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ORIGINAL ARTICLES

SOME PROBLEMS IN THE PATHOLOGY OF SYPHILIS.[1]

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It is proposed in the present paper to discuss some of the phases of syphilis which have resulted from the intensive investigations of the past ten years. These problems include the question of immunity, a few of the most striking anatomicopathological changes met with in the disease, as well as its effects on the cardiovascular and nervous systems, and the lessons to be deduced from the knowledge which has been gained.

Immunity. One of the most interesting and perhaps least understood problems in the pathology and biology of lues is the question of immunity. Formerly it was taught that like many of the other infections one attack of syphilis conferred a lifelong immunity, that a syphilitic mother might transmit an immunity to her child, while, conversely, the mother of a syphilitic child was rendered insusceptible to the disease, as postulated in the well-known laws of Profeta and Colles-Baumès. Since the work of Neisser, Finger and Landsteiner, Levaditi, Uhlenhuth and Mulzer, and others, however, our conception of immunity in syphilis has undergone considerable modification.

Investigations along these lines and in microbiology have shown that syphilis is closely allied with the protozoal affections, especially

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those caused by trypanosomes and piroplasomes. These diseases differ from those of bacterial origin in the manner in which they respond to the introduction of organisms into the system. While in the great majority of infectious processes acquired immunity is expressed by a protection more or less absolute against a new attack and the disappearance of the causal agent from the body, or its innocuousness to the host if it persists, diseases of protozoal origin behave in a different way. Levaditi has demonstrated, for instance, that animals suffering with a spirillary infection are immune to a new inoculation. Their serum has a high antibody content, but the blood still harbors parasites and is capable of producing a fresh infection in healthy animals. So with the serum of guinea-pigs inoculated with Nagana or Surra trypanosomes. This is trypanocidal for these organisms *in vitro*, but *in vivo* they have acquired an insensibility to the trypanolytic antibodies, for the blood and tissues of the animals still contain parasites. The same is true of human subjects suffering from sleeping sickness in whose serum trypanolytic, agglutinating and other protective bodies have been demonstrated. Carrying the analogy to syphilis we find that an individual may harbor spirochetes for forty or fifty years, while his skin and mucous membranes exhibit an insusceptibility to re-inoculation under natural exposure. However, as soon as he is freed from his infection he is again in as susceptible a state as he was prior to his first attack.

It is a well-known clinical observation that after the development of the initial lesion a syphilitic is immune to a fresh infection. Why have the integument and mucous membranes ceased to react to organisms introduced from without when they are susceptible to their action from within? The opinion has been generally held that for infection to take place one of the first laws of its requirements is fulfilled by a surface covered by squamous epithelium. The earlier experiments on animals seemingly corroborated this view, for inoculations were only successful where scarification of a squamous-celled area was performed. Improved laboratory technique has, however, overcome the difficulty, positive results now being obtained in animals by the introduction of the virus into the testicle, peritoneal cavity, under the skin or directly into the circulation, especially the heart.

In human syphilis, while it is more usual for the general infection to be preceded by the development of a primary lesion, somewhere on the cutaneous or mucous surface, it is not rare for the local reaction to be altogether absent. To illustrate: a male nurse in my hospital service pricked himself with a needle used for obtaining blood for the Wassermann test directly after he had withdrawn it from the vein of a patient with florid syphilis. He was carefully watched for the development of a chancre at the site of injury, but the first macroscopic manifestation was a late secondary papule

on his foot. Similar cases are reported in the literature. Another instance is exemplified in a personal communication by Dr. Dade, in which he related the infection of a young girl by blood transfusion. Her brother, whose blood was used for the treatment of her anemia, was at the time of the operation in the second incubation period of the disease. She in due course of time developed a secondary rash. Congenital lues is a further example of syphilis without the development of an initial lesion. Neisser came to the opinion, from his many experimental observations, that in certain cases infection might take place through the integument without visible or even microscopic changes, the organisms gaining access to the lymphatic or blood stream direct.

When spirochetes are successfully implanted, what takes place? As soon as they have become acclimated to changed nutritional conditions at the site of inoculation, as shown by Levaditi and Yamanouchi, they multiply, call forth microscopic changes in the cutaneous vessels, and enter the lymph and blood stream. This is known as the first incubation period and varies in length in different subjects. Just how far the organisms penetrate beyond the local sore and satellite lymph nodes in human subjects in this stage is not known, but it has been demonstrated by Neisser that the spleen and marrow of inoculated monkeys contain virus thus early in the infection. Now, as the chancre is forming a peculiar reaction on the part of the host is also developing. At first it is so feeble that the individual is for some time susceptible to re-inoculation. In animals it has been found that superinfection is possible if made eight days before the evolution of the primary lesion. Not rarely we see patients with multiple chancres. In some instances they develop simultaneously as the result of multiple inoculations; in others they appear successively either from auto-inoculation or contamination with a fresh virus. Human and animal experiments are at one in showing that superinfection lesions do not develop in the typical manner of those implanted on a virgin soil. Their incubation period is shorter and their clinical characteristics simulate those of the stage the patient is in at the time; that is, papular if close to the secondary period and ulcerative if in the tertiary stage. In other words, they are the expression of an altered tissue reaction. The hypothesis has been advanced by Krause and Volk that this immunity has a regional development, beginning at the site of the primary sore and progressively involving the mucous and cutaneous covering. Neisser has suggested that the susceptibility to re-infection returns in an inverse manner.

During the second incubation period the refractory state continues to develop until it attains its maximum with the outbreak of the secondary rash. Even now, however, it is only relative, for laboratory experiments have yielded positive results if special methods are employed, namely, larger amounts of active virus

introduced subepidermically. From a clinical stand-point, however, this refractory state, or anergy—the term usually applied—is complete as far as ordinary infection is concerned, disappearing only with the cure of the disease, when the patient is again in a receptive condition.

It has been demonstrated further that the anergy is a specific one, the attempts of Neisser, Baermann, and Halberstädter to induce it by inoculation with Spirocheta pertenuis, of Hidaka with Spirocheta duttoni, and of Uhlenhuth with Trypanosoma lewisii having proved futile. None of these infections protected against that of syphilis, while, on the other hand, luetic animals were all susceptible to frambesia, relapsing fever, and dourine. Little is known of the nature of this state of resistance or how it is brought about, whether by the tissues, cells, the serum, or intermediary organs. Organisms or their toxins when introduced into the body behave as antigens and stimulate the formation of antibodies which are specific for that particular bacterium. These antibodies are of the nature of antitoxins which neutralize the toxins; opsonins which lead to the ingestion and destruction of the organisms by the leukocytes; agglutinins which cause the organisms to adhere together and probably also bring about their destruction and bacteriolysins which cause their dissolution. From the contributions to this branch of research in lues the conclusions are that substances of a parasiticide nature do not develop in the course of the disease. At the most, says Neisser, we can reckon with complement binding and agglutinating substances of a specific nature. Levaditi, however, argues that since the spirochetes even before the evolution of the primary lesion may penetrate to the hematopœtic organs, they act like true antigens and their products of secretion stimulate the formation of antibodies. He assumes an analogy between these immune bodies and those of related diseases, where bacteriotropic substances and opsonins ensure destruction by phagocytosis. *Pari passu* with this antibody formation the skin acquires a refractory state to exogenous spirochetes, the biological changes being sufficiently advanced at the close of the second incubation period to determine the character of the reaction. He has offered two attractive hypotheses to explain why the skin which is resistant to exogenous spirochetes reacts to endogenous organisms, (1) by a generalized eruption, and (2) after a varying latency, by local and destructive lesions. His assumption is that for a time the immune bodies hinder the multiplication of the parasite, but with the enfeeblement or disappearance of the former the virus gains the ascendency, generalizes itself, and produces the secondary eruption. Or the spirochetes are vaccinated, so to speak, against the immune bodies, and, becoming resistant to these defensive substances, they succeed in multiplying and provoking the exanthem.

It is a well-established clinical fact that the early cutaneous

lesions are superficial and generalized, that with each relapse they show a tendency to localization and grouping with involvement of the deeper structures until we reach the tertiary stage with extensive destruction. Since it has been shown that these differences are not inherent in the specific virus but in the tissues of the host brought about by prolonged contact with the causal agent, the term allergy or, according to Neisser, Umstimmung has been proposed to explain the biological change which has taken place in the tissues. In the primary and secondary stage, when the organisms are numerous, the host is refractory; in the tertiary stage when they are few in number an anaphylactic state exists, the tissues are frail and more readily undergo necrosis. This is also seen in superinfection in tertiary syphilitics when the lesion corresponds to that type, and in the luetin reaction, which is especially applicable in congenital and tertiary syphilis, depending for its result on the hypersusceptibility of the tissues. In tuberculosis a similar condition is encountered. Erythema induratum, for instance, is caused by few organisms, and yet clinically presents extensive destructive lesions. Another clinical type is seen in large and deep ulcerations of the extremities in tuberculous subjects, all treatment, excepting surgical, being of little avail. The writer has recently had under his care a young man with glandular tuberculosis in whom the entire right leg was involved, necrosis extending through the musculature and laying bare the bone.

The immunity processes as outlined in the foregoing considerations are subject to modification under treatment. Where treatment is intensive and yet not sufficient to effect a complete cure it would appear that the anaphylactic stage is hastened, for it has been repeatedly claimed that specific remedies given early in the disease tend to produce relapses of severe local intensity. Herein we find the basis for the contention that salvarsan has changed the course of the disease, and when not given in sufficient doses to sterilize the patient, tertiary lesions appear much earlier than when the affection is permitted to run its course with the gradual establishment of a defensive mechanism, and consequently a longer refractory state. In so-called malignant syphilis we must also seek the cause in a precocious anaphylactic condition of the tissues rather than in the type of the invading organism, the reason usually evoked for this form of the infection. It has repeatedly been reported that spirochetes are numerically few in such lesions and that successful inoculations are relatively rare.

As accumulated evidence has shown that individual immunity is only relative, so racial immunity in the strict sense of the word does not exist. Lesser has said that neither race nor climate makes any difference in the receptivity of the virus of syphilis. Furthermore, it has been demonstrated that the children of syphilitic parents do not develop an immunity. Such children may be frankly

syphilitic at the time of birth or they may be in the latent stage for years (syphilis hereditaria tardiva). Or if they escape infection and acquire the disease later on, it has never been observed to have a milder course. Gluck reports that although syphilization is almost general in Bosnia, extra-uterine acquired lues is not rare. He noted 10 per cent. of cases of recent syphilis in children under fifteen years, one-third of whom were only five or six months old.

While complete statistics and comparative studies on the course of the disease in the different races are not available, the investigations made have revealed some interesting facts. Neisser found that in the Malays primary and secondary syphilis was insignificant. Treatment is therefore deferred and the percentage of cutaneous tertiary manifestations is proportionately large. He seldom met with visceral or nerve manifestations, and never encountered tabes or paresis. In Java and the tropics generally Europeans suffer more severely than the natives, which is attributable to unfavorable climatic conditions and changed mode of living. According to Quennac, Europeans, Hindoos, and Arabs in Africa suffer severely while the negroes only have mild attacks. In Central America, Rutschuh reported severe syphilis in the whites and negroes in contradistinction to the Indians and half-breeds who only suffered mildly. Among the Indians in the United States the infection is very destructive in some localities, as cited by Dr. Hrdlička, while it runs a mild course in certain other tribes. This authority also states that he has never seen tabes or paresis among the Indians, although they suffer from other forms of mental disease. As to the negroes in our country the writer has a personal communication from Dr. Green, of Milledgeville, Georgia, in which the statistics collected by him show that 5.27 per cent. of negroes suffer from paresis as against 2.12 per cent. of whites. Tabes is rare in this race.

It is often said that the European pandemic at the end of the fifteenth century was an exceedingly malignant one. This claim is now challenged by syphilographers that the disease was malignant in the present sense of the word, that is, ulcerating lesions in the early secondary period, but rather that many of the so-called cases were ordinary ulcerating tertiary forms. Instead of malignancy *per se* and a racial susceptibility, other factors are called into account, as the undeveloped treatment, wars, famines, etc. Neisser suggests that spirochetes in their continual passage through human beings lose in virulence, or that the treatment which the patient receives so modifies the virulence that when such modified spirochetes are transmitted they produce a modified disease.

HEREDITY. The question of the transmission of syphilis to the offspring is a very complicated one, and still far from clear. While the accession of serological knowledge has presented a partial solution, there still remain certain clinical phenomena for which no satisfactory explanation can be given.

The opinion is gaining on almost every hand today that germinal infection on the side of the father does not take place, but that the mother, infected by the father either before or at the time of conception, transmits the disease to the fetus through the placenta. Is this view tenable on the ground of our clinical and laboratory observations?

Disease of the testicles during the secondary stage is not common, although it has been demonstrated by animal experiments that this organ is one of the seats of election of the syphilitic virus. Later a diffuse orchitis is more frequent, and during the tertiary stage gummata are not uncommon. As to other lesions of the genito-urinary tract which might harbor spirochetes little is known.

In the transmission of syphilis the results depend upon the intensity of the infection, which intensity weakens with time.

In the secondary stage it is most active, so that a man is almost certain to infect his wife. If she becomes pregnant early abortion will result. Such a woman, if untreated may abort later, then have a stillborn child or a living child with active syphilis, and finally, after eight to twelve to twenty years, healthy children. Such women are obviously syphilitic. On the other hand, there is the group of women who have been free from the clinical manifestations of the disease but who have had several miscarriages or children with unmistakable signs of the infection. These women, according to Colles-Baumès law, have not syphilis but are immune to syphilis. What has taken place that prevents such a woman from developing a primary sore or a secondary rash and still has rendered her insusceptible to the disease? Is it because she has the infection or because Wassermann substances or antibodies are passed through the placenta? In other words, must we conclude in view of the positive Wassermann reaction that her tissues are harboring living spirochetes which without treatment are overcome by the defensive mechanism of the patient or does she simply receive Wassermann-producing substances?

Serological research has in the main overthrown Colles' and Profeta's laws. It has been demonstrated by a host of investigators that the majority of women apparently healthy who give birth to syphilitic children have a positive Wassermann reaction and are therefore in the latent stage of the disease. Furthermore, Baisch, Trinchese, and Weber constantly found spirochetes in the maternal portion of the placenta and in the intervillous spaces even in negatively reacting women. The claim then that Wassermann-producing substances pass over from the fetus to the mother had to be dismissed as the persistence of the reaction after birth was strong presumptive evidence of the presence of living spirochetes, their demonstration in the placenta supporting the contention. The transmission of organisms to the fetus by way of the placenta finds its analogy in other diseases, such as smallpox, relapsing fever, and

tuberculosis. In tuberculosis this takes place only in advanced and florid cases in contradistinction to lues, where no clinical evidence of the disease may be present, multiplication of the spirochetes probably taking place through the impetus given by pregnancy. It is interesting to note in passing that Uhlenhuth found typical testicular lesions in the young of a syphilitic mother rabbit, illustrating that the organisms pass through the placenta. Varying degrees of latency are met with. In some women a negative Wassermann in the blood is accompanied by a positive reaction in the colostrum of the breast, or the placental blood may be stronger than the rest of the serum. The evidence submitted in favor of maternal transmission is convincing, but the question as to how the mother received her infection is not so easy of solution. Is she inoculated prior to or at the time of conception or later? Do the organisms penetrate the ovum or do they enter the tissues of the mother without the production of the usual sequence of symptoms? It has been shown experimentally that the semen of latent syphilitic men may from time to time contain spirochetes. As many of these patients have had more or less treatment, it has been suggested that an attenuated form of the disease is transmitted to the wife. There are two ways in which paternal transmission could take place. In the one we may assume that the parasite is carried in the head of the spermatozoön and with it penetrates the ovum. As the organism is three times the length of the spermhead this possibility is dismissed by the majority of syphilographers. The other alternative is that the spirochetes are free in the semen and with it enter the egg cell. Such an event it is believed would have an untoward effect on the fertilized ovum, as it has been shown that the disturbance of a single blastomere in lower vertebrates is sufficient to arrest development or cause malformation, and the regenerative powers are greater in these animals than in the higher vertebrates (Weber).

Latency. What is our present conception of latency in syphilis? During these periods of apparent quiescence does the defensive mechanism hold the pathogenic agent in abeyance or is some pathological process insidiously undermining tissue in some part of the body? The application of the Wassermann reaction has materially changed our views since the demonstration in a large number of so-called latent syphilitics of involvement of the aorta and the central nervous system. It has been shown that such patients may have a chronic meningitis for years without producing obstrusive symptoms, and a limited aortitis may persist for a long time without making its presence known either subjectively or objectively. Aside from gummatous involvement of the viscera little is known of the effects of the infection on the various organs. Where must we seek the explanation of persistent Wassermann reactions in cases intensively treated in whom involvement of the central nervous system

and the heart and aorta can be excluded? A solution will probably be reached when the nature of the Wassermann reaction is fathomed, but on *a priori* grounds if a focus in the aorta or nervous system is capable of keeping up a positive reaction indefinitely, it is reasonable to assume that a similar process in one of the viscera may be provocative of a like result.

It is often asked where the spirochetes are lodged during the latent period. A number of investigators have urged that during this stage, resting forms of the organisms are harbored by the lymph nodes or blood-forming organs. Present knowledge does not support the theory of a cycle of evolution with the power to produce lesions according to the stage of its development. Spirochetes recovered from any source whatever—chancre, mucous patch, or gumma—the blood, nervous system, or viscera have all shown similar morphological and practically the same biological characteristics.

The relation of trauma to the localization of specific lesions has been so well appreciated by the medical profession that it is given a prominent place as an etiological factor. The query naturally arises as to whether the spirochetes in such cases have remained *in loco* since their primary deposition or are carried there by the blood after injury to the tissue. Pasini found spirochetes in an atropic and pigmented spot two years after the involution of a papular syphilide, while Hoffman demonstrated them in scar tissue of chancres long after their regression. Levaditi and Yamanouchi were able to recover them from the cornea of a rabbit one hundred and thirteen days after the keratitis had healed and at which time a recurrence took place. The so-called chancre redux is interpreted by many as the result of organisms which have escaped destruction rather than as a superinfection with a new strain. Neisser has demonstrated that spirochetes may be present in the skin without producing any macroscopic changes, and more recently Whartin has called attention to their presence in the heart without exciting tissue reaction.

Studies on the infectiousness of the blood in the various stages of syphilis have supplied us with the following data: In 19 cases of primary syphilis, Uhlenhuth and Mulzer obtained positive results in 16 rabbits injected with 2 c.c. of defibrinated blood into the testicle; in 36 cases of early secondary syphilis, 27 positive results, and in 15 cases of latent syphilis 2 successful inoculations. One of the latter was with the blood from a woman whose infection was four years old and who eighteen days before had given birth to a syphilitic child. Lieberman also succeeded with the blood from a woman whose primary lesion dated back four years and who six weeks before had given birth to a luetic child. Frühwald reports 2 cases: In one the disease had existed for one year, the Wassermann was positive and the patient had had two doses of

neosalvarsan, each 0.75 gm.; in the other the infection was one and a half years old, the Wassermann was positive, and the patient had received two doses of neosalvarsan of 0.6 gm. each.

Numerous attempts have been made with the blood of paretics and tabetics, but with little success. Levaditi demonstrated spirochetes in the blood of one patient with paresis, and Graves reported positive results with blood from two paretics. Ellis' experiments to confirm these findings gave constantly negative results.

The above facts are in accord with the clinical teaching that the blood of luetic individuals is infectious during the active primary and secondary stage, and that this diminishes with the age of the disease. Exceptions to the innocuousness of the blood of latent syphilitics are seen in the occasional infection of a surgeon in his operative work on an individual in this period of the disease. It is to be inferred therefore from clinical and laboratory experience that under conditions of which we are at present ignorant, spirochetes may reach the circulation from some focus in the body. In certain cases this may precede the cutaneous relapse, in others it is accompanied by no visible manifestations. Kraus has called attention to febrile attacks as the only symptom of latent lues, and suggests the spirochetemia as a possible explanation. An analogy is found in trypanosomiasis where the parasites may disappear spontaneously from the blood and reappearing give rise to an eruption and fever. Moreover, a latent period of three years may ensue before the nervous symptoms appear.

Pathological Anatomy. The predilection of syphilis for the vascular system is noted almost from the inception of the disease in the involvement of the cutaneous vessels at the point of inoculation. Here the pathological process consists of an endarteritis, later a panarteritis, with a characteristic inflammatory infiltration. Excepting the macule all the lesions succeeding the chancre show a marked affection of the vessels, especially those of the late secondary and tertiary stages. The formation of giant cells so frequently encountered in the secondary papule, the nodular syphilide and gumma may be traced to a vascular genesis, while the extension of serpigenous lesions may be explained by the progressive thrombosis of the vessels.

A study of the pathological anatomy of syphilis shows that fundamentally the reaction is on the part of the fixed connective-tissue elements, the labile constituents coming into play locally only secondarily. The chief cells are the lymphocyte and the plasma cell, the latter believed to be a derivative of the former and the antecedent of the fibroblast. It has been shown by Hazen that a circulatory leukocytosis is present in untreated secondary cases, sometimes as high as 20,000 white cells. The neutrophiles are absolutely and relatively increased and the percentage of eosinophiles is higher.

Under treatment there is a slight drop in the total count, with a marked relative increase in lymphocytes which under treatment may run as high as 65 per cent.

The syphilitic process is essentially a granuloma having its origin in the perivascular lymphatic spaces. In the primary lesion the main changes are found in the cutis, the very earliest of which are in the new formation of capillaries and the grouping about these and preëxisting vessels of lymphocytes and plasma cells. At first they mantle the vascular structures as a "coat-sleeve" infiltration, but as the lesion grows older, spread out and become diffuse. The endothelium of the capillaries is swollen and proliferated so that the lumen is narrowed or altogether occluded, and in the larger vessels with an external coat there is in addition evidence of inflammation and an increase in thickness. In some instances giant cells are found. From the newly formed granulation tissue, connective tissue is formed which later scleroses and leads to induration. Owing to interference with nutrition, regressive metamorphosis sets in. The epidermis presents a varied picture, depending on whether there is pressure from the infiltrate or retrograde changes with erosion and ulceration.

In the secondary stage the disease is characterized by a succession of eruptions and a general adenopathy. Ehrmann has said that the distribution of secondary syphilides is governed by the branching of the vascular stems. The roseola or macular syphilide under the microscope shows very few changes, being simply an erythema with dilatation of the vessels of the papillary body and adjoining corium and an infiltration of lymphocytes and plasma cells about them. In the papular or lenticular syphilide we find in the cutis a circumscribed lesion made up of lymphocytes, plasma cells, and proliferated fibroblasts, all in close relation with the vessels which show the characteristic changes. Lichen syphiliticus owes its peculiar features to localization, namely, distribution about the pilo-sebaceous apparatus. Here the process surrounds a hair follicle and extends deeply into the corium. Its structure is like that of other lesions, with usually abundant giant cells of vascular origin. The epidermis in all lesions of this stage shows only secondary changes. It may be thinned from pressure of the granulomatous tissue beneath or there may be edema with an increase in thickness and scaling. In condylomata papillomatous overgrowth is a marked feature. Pustular and suppurating syphilides usually signify extraneous inoculation with pus-producing organisms. The pigmentary syphilide, or leukoderma syphiliticum, according to Ehrmann, is due to chromatophores, the pigment passing from them to the basal layer of the epidermis.

As a rule, secondary syphilides undergo spontaneous absorption. Microscopic residua may, however, persist for a long time. Their connection with local relapses has been suggested.

The type of lesion of the tertiary period is the gumma. The process consists of an infiltration of lymphocytes, plasma cells, and proliferated connective-tissue cells about the vessels, newly formed and old, which are the seat of an endarteritis and panarteritis, and give rise to giant cells. Caseous degeneration usually begins in the centre of the granuloma, or in some cases it may be fatty or mucoid in character. The last mentioned is most often found in bones. The necrotic areas liquefy and are absorbed or discharged, the usual procedure being gradual absorption, with formation of cicatricial tissue, the contraction of which leads to deformity. It is believed by many that the fibrosis is not purely a process of repair or due to the irritating action of necrotic tissue, but that there is also a syphilitic element. The plasma cell thought to be the precursor of the fibroblast has been credited with being more than a passive participant. The late nodular or tubercular syphilide is in reality a gumma, situated more superficially in the cutis. The serpigenous lesions which also belong to this stage are made up of groups of nodules situated about the cutaneous vessels, the thrombosis of which probably explains the progressive character of the lesion.

Syphilitic phlebitis is relatively infrequent, occurs usually in the veins of the lower extremities, and is of minor importance. Arterial disease, however, is very common and of serious import, the vessels especially attacked being the aorta, the cerebral, pulmonary, subclavian, femoral, and popliteal arteries. Owing to disease of the walls, vasomotor response is impaired or lost, and where there are obliterative changes due to endothelial proliferation or secondary thrombosis, interference with the blood supply and impairment of nutrition. While the brain and the heart suffer more severely in this respect, other organs and the vessels of the extremities are not exempt. Several years ago the writer had under observation a case of gangrene of the leg consecutive to a syphilitic thrombosis of the femoral artery (Fig. 1). The patient was a colored girl, in the City Hospital, upon whom several amputations were made, after each of which the gangrenous process developed and spread. A picture closely simulating Raynaud's disease is also met with as the result of luetic involvement of the vascular supply of the extremities, and in several cases of symmetrical cutaneous atrophy which I have had under my care the syphilitic element was the predominant feature.

Aortitis. It is only within the last decennium that the syphilogenic nature of aortitis or mesaortitis has been generally recognized among internists and syphilographers. During this period the development of the Wassermann reaction and roentgenology, as supplementary to the physical examination, have shown us how widely prevalent the disease is among individuals who have had a syphilitic infection.

As to its frequency of incidence, Chiari found the condition present in 59 per cent., Fahr in 29 per cent., and Fraenkel fifty-three times

in 102 cases of constitutional syphilis. Stadler, whose statistics cover 256 cases, demonstrated the disease in 82 per cent., and of 211 of this number it was the cause of death in 117. Staub found an aortitis in 82 per cent. of paretics which came to autopsy, Buder in 84.5 per cent., and Alzheimer in 74 per cent. The findings of Rach and Wiesner show that in congenital syphilis, changes in the aorta or pulmonary artery are seen in 67.4 per cent. Lenz states that in large cities 25 per cent. of all syphilitics die from aortitis (angina pectoris, aortitic insufficiency, aneurysm) as against 3 to 4 per cent. from paresis, 1 to 2 per cent. from tabes, and 10 per cent. from all other syphilitic affections, as of the brain, liver, kidneys, etc.

FIG. 1.—Syphilitic thrombosis of femoral artery. Transverse section of artery, showing thrombus and thickening of arterial coats.

Mesaortitis has been defined by Doehle, Heller, and others as a specific inflammation of the adventitia and media which terminates in cicatricial deformity. As a rule, there is a combination of processes so that cicatrization may be present in one part while active inflammatory lesions are found in another. The disease shows a decided preference for the ascending portion of the aorta and the arch, the explanation being that the impact of the blood is greater here than in the rest of its extent, following the well-known law that syphilis localizes where trauma has produced a *locus minoris resistentiæ*. In contradistinction, atheroma selects the lower portion of the aorta where the mechanical element is of slighter moment. Stadler could find no relationship between an increased

blood-pressure or marked variations in pressure. Strümpell favors a summation of injurious agencies, as the noxious influence of alcohol and tobacco, with consequent lowering of resistance of the vessels.

Grossly the aorta gives a characteristic picture (Fig. 2). The inner surface shows isolated or confluent elevated, wrinkled, grayish, and translucent sclerous areas, with puckering or cicatricial pitting, or again radiating ridges with depressed cicatrices between. The intima over the affected areas preserves its glistening appearance. The thickness of the artery varies in different portions, so that while indurated and sclerotic at one point it is thin and translucent at another. Depending on the extent of involvement, dilatation is present. This may be uniform throughout the length of the thoracic portion or appear as small aneurysmal pouchings or a true saccular aneurysm. All transitions are found. Ordinarily it is not difficult to differentiate this condition from arteriosclerosis in the absence of fatty degeneration and calcification. However, in old subjects there may be a combination.

FIG. 2.—Syphilitic aortitis, showing characteristic changes in the walls of the vessels, transverse rupture, and dissecting aneurysm into coats of the aorta. (Specimen of Dr. John H. Larkin.)

In the beginning the lesion is often confined to the vessel in proximity to the aortic valves. Later it extends to them and gives rise to insufficiency, which condition is very frequent. With the extension of the process the ascending aorta and the arch are involved. Not rarely changes are also noted about the mouths of the larger branches of the arch, causing narrowing of the left carotid, innominate, and subclavian arteries, which localization is significant from a clinical point of view. With involvement of the aortic ring the mouths of the coronary arteries are also considerably reduced.

The relation of syphilis to aortitis was for a long time disputed. On the one hand investigators classed it with parasyphilis because of the difficulty of demonstrating spirochetes, its indurative or

fibrotic tendencies, and indifferent results from treatment. On the other, which has the support of recent examinations, it was classed with active syphilis. The demonstration of spirochetes in the aortic wall by Reuter, Schmorl, Wright, Richardson, and others in acquired syphilis, and by Wiesner and Rach in congenital, together with the microscopic picture of gummatous lesions, and a positive Wassermann reaction in about 80 per cent. of cases, definitely places the affection in the category of active syphilis. It is difficult to demonstrate the organisms even in comparatively recent and active lesions. This, however, does not militate against their syphilitic nature, as they are equally difficult to demonstrate in cutaneous

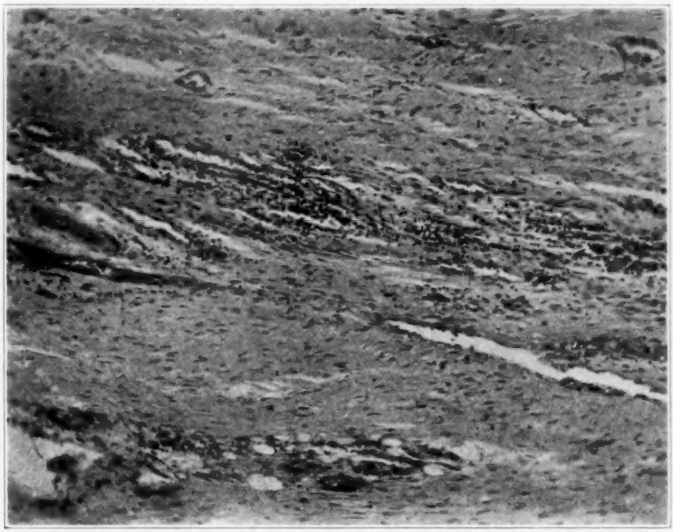

FIG. 3.—Early stage of aortitis, showing characteristic lymphocytic and plasma-cell infiltration about the small vessels in the adventitia.

gummata. In both the tissue is probably in a state of altered reactivity, so that numerically few organisms are capable of bringing about the necrotic change. The striking changes are in the media, although the disease begins in the adventitia. Miliary gummata undergo necrosis and are replaced by cicatricial tissue. In the adventitia in recent processes an inflammatory infiltrate of lymphocytes and plasma cells is localized about the vasa vasorum (Fig. 3), while in older ones only fibrotic changes may be left (Fig. 4), the nutrient vessels themselves being the seat of an obliterating endarteritis, such as is found in syphilitic lesions elsewhere in the body. The elastic tissue, and this is characteristic of luetic disease

of the larger vessels, is either fragmented or has entirely disappeared. The intima shows no change at all or various grades of a compensatory thickening. On the question of genesis of the early changes there is some dissonance of opinion. Doehle, Heller, Backhaus, Saathoff, and others trace the beginning of the disease to the vasa vasorum. They claim, primarily, a swelling of the endothelium of these vessels in the middle third of the media to large epitheloid cells, which lead to an obliteration with secondary regressive metamorphosis of the aortic wall. Marchand, Beneke, Arnsperger, and others not corroborating these findings incline to the view that the medial changes are primary, the virus so injuring the elastic lamellæ

FIG. 4.—Later stage of aortitis, showing advanced sclerosis of the vessel walls.

that they succumb to the pressure of the blood. The difficulty of determining the genesis with positiveness even early is apparent, for, as Stadler points out, a simple infiltration of the vasa vasorum may also occur under the influence of the toxins of alcohol and other infections. Benda describes two forms of aortic disease. In the one submiliary lesions without necrosis which cicatrize and leave none or only a very slight deformity of the vessel wall, in the other typical gummata, with central necrosis, the scarring of which leads to typical sclerotic changes in the wall.

The clinical diagnosis of aortitis is often extremely difficult. Limited and circumscribed changes of the ascending portion without involvement of the ring are, as a rule, not accompanied by sub-

jective or objective manifestations. Such patients may be observed for a long time without eliciting signs pointing to the condition, Roentgen-ray examination also being negative. Only when a greater area is involved especially more or less of the circumference are there symptoms suggestive of disease, namely, pain, dyspnea, and tachycardia on slight exertion, increased blood-pressure, weakness, and easily induced fatigue.

The pain is often the primary and predominant symptom, although frequently it is lacking or indefinite. It is characterized as a dull aching or a feeling of pressure under the sternum, with pain radiating to the side of the chest, the back, and the arms. Disease of the innominate, carotid, and subclavian may be attended by a condition simulating intermittent claudication of the lower extremities, with weakness, radiating pain, and sensory disturbance. Periodic or continuous headaches, often with vertigo, accompany involvement of the mouth of the left carotid, and where the coronary arteries are the seat of disease the attacks are anginal in character. There appears to be no satisfactory explanation for the origin of the pain. Thoma referred it to injury of the larger and smaller nerve trunks as well as irritation of the Pacinian bodies in the aortic wall. Huchard attributes it to a peri-aortitis, and the neuralgic pains in the chest and shoulder to the changed relation of the subclavian to the brachial plexus. Longcope came to the conclusion that the anginal attacks were due to reflex disturbances set up by the syphilitic process involving the root of the aorta, the paroxysmal dyspnea being regarded as an acute bronchiospasm.

When does the aortic disease begin? Obviously this is difficult to affirm, as the disease in the majority of cases is insidious in its onset, the first symptoms appearing only when the affection has made some progress. In assuming that involvement takes place at the close of the primary stage when there is a general dissemination of the spirochetes, we are confronted with the same problem as when we endeavor to establish the time of infection of the central nervous system. Palpitation, arrhythmia, tachycardia, and disturbances in the pulse rate frequently occur in early secondary syphilis, which has been adduced as evidence that involvement takes place at the time the disease is a spirochetemia. The publication of fatal cases shortly after infection also inclines to the view that involvement takes place early. Brooks recorded perforation of an aneurysm before the secondary rash had fully appeared, and another case with a fatal aortic lesion within six months of infection. Longcope cites two patients who died from the effects of syphilitic aortitis four years after the appearance of the chancre. Stadler publishes two cases in whom death occurred five years after infection. The first patient, aged twenty-nine years, showed at autopsy a fibrous aortitis and aneurysm. The second, aged twenty-seven years, the objective and subjective signs of an aortitis.

He further studied 12 postmortem cases of severe secondary and tertiary syphilis in patients under thirty years of age. He assumed on account of the youth of the subjects that the infection could not have been of long standing, but in none were changes of syphilitic aortitis demonstrable.

The writer has recently investigated, in his private practice, all latent syphilitics, especially those with a persistent positive Wassermann, for the occurrence of cardiovascular disease, and in a large percentage has found the existence of such a lesion.

The average age at which the disease appears is forty-seven to forty-nine years, but it is not rare to find it in much younger patients. Aortic disease in general makes slow progress, for Weintraud, Stadler, and others give the average lapse of time as twenty years, the interval vacillating between five and forty years. The disease usually runs a fatal course in about two years after the development of the symptoms. The importance of early diagnosis is, therefore, apparent, especially in view of the fact that the affection is a manifestation of active syphilis and amenable to treatment. In 95 cases of aortitis collected by Benda the termination was as follows: In 9, coronary stenosis; in 22, aortic insufficiency; in 37, combined coronary stenosis and aortic insufficiency; in 27, aneurysm. In a total of 248 cases he found aneurysm forty-eight times.

The relation of cardiovascular affections to tabes has for a long time occupied the attention of clinicians. According to Lesser's statistics in 96 cases of tabes come to autopsy, aneurysm of the aorta was found eighteen times. A review of the literature shows that the coincidence of tabes and aortic insufficiency is most frequent. Rogge and Ruttner report the association in 6.5 per cent.; Rogge and Müller in 10 per cent.; Stintzing in 3.8 per cent., and Stadler in 6.2 per cent. of all cases of well-developed tabes. The latter did not include his cases of incipient tabes; in manifest tabes which came to autopsy, however, he found disease of the aorta in almost all. Rogge and Müller have called attention to the cause of sudden deaths in tabetics as being due to lesions referable to the central nervous system but to sudden cardiac insufficiency or rupture of an aneurysm. The so-called cardiac crises are in reality attacks of angina pectoris, due to changes in the coronary arteries.

Strümpell has emphasized the surprisingly frequent presence of rudimentary tabes in patients who seek medical advice for symptoms referable to the heart. Many of these cases show only pupillary changes, such as narrowing, irregularity, and fixation to light. Only one pupil may be affected, as in a case cited by him with severe endocarditis, myocarditis, and aortic insufficiency. The reflexes are only slightly altered or the Achilles reflex alone lost and the patellar reflex exaggerated. Observing these cases over a long period of time, weakening and gradual disappearance of the

reflex may be noted. In general, symptoms of aortic disease appear later than the earliest tabetic manifestations. Rogge and Müller are of the opinion that tabetic symptoms average four and a half years earlier than those of the circulatory apparatus. It is probable that it is not a later involvement, only that the condition has a longer latency and therefore manifests itself later.

The writer has under treatment at the present time several patients with tabes and concomitant aortitis. One of them, with optic atrophy, has an aneurysm. Five others, in whom the tabetic symptoms have existed on an average of eight years, show a marked sclerosis of the aorta. In a paretic, Roentgen-ray examination shows dilatation of the ascending aorta and in a case of cerebrospinal syphilis, with cardiac symptoms developing four months ago, a small aneurysm. In another patient, aged thirty-one years, who had had an attack of hemiplegia four years ago, signs of aortitis have developed within the past few months. The Roentgen-ray plate also show a marked sclerosis.

For the following interesting postmortem examination and also some of the illustrations which accompany this article I am indebted to Dr. John H. Larkin, Director of Pathological Laboratories, Department of Charities, New York City:

J. E., aged forty years. The patient was admitted to the City Hospital (service of Dr. Evan Evans) the latter part of 1913 for sciatica. After a few weeks he was discharged and five months later re-admitted, at which time in addition to the sciatic pains he complained of girdle pains. Lumbar puncture showed thirty-eight cells, an excess of globulin, and a strongly positive Wassermann. His serum was also positive. A diagnosis of tabes without clinical evidence, excepting the girdle pains, was made. Further examination, including Roentgen-rays, revealed an aneurysm of the ascending aorta. He was placed on salvarsan and mercurial treatment, which reduced his cell count and reversed the Wassermann in the fluid, but had no effect on that of the blood. The patient died suddenly from a rupture of the aneurysm into the thoracic cavity. Microscopically the aorta showed a characteristic picture with a round-celled infiltration in the adventitia. The interesting feature of the findings in this case was in the cord, which showed an involvement of the pia-arachnoid with a round-celled infiltration about the small vessels and an insular degeneration of the posterior nerve roots (Fig. 5). The posterior columns were unaffected.

Nervous System. With the acquisition of more exact knowledge our ideas concerning syphilis of the nervous system have undergone considerable revision. The present views based on clinical and laboratory investigations may be formulated as follows: Infection of the central nervous system probably takes place in the early stage of the disease with the generalization of the virus. Accumulated clinical evidence points to meningeal involvement during the first few

months, in some cases before the appearance of the cutaneous eruption. Lumbar puncture in the hands of different investigators has elicited varying results. Thus, Ravaut found the spinal fluid in secondary syphilis abnormal in 67 per cent. of cases, Altmann and Dreyfus in 78 per cent., Nonne in 40 per cent., and Swift and Ellis in 36 per cent. The writer's findings, based on the examination of cases in the secondary stage with and without cutaneous lesions, showed meningeal involvement in less than 20 per cent. Fournier's dictum that patients in whom secondary symptoms are overlooked or very mild later show involvement of the central nervous system has been reiterated again and again. This led Finger

FIG. 5.—Insular sclerosis posterior nerve root, with accompanying meningitis. Posterior columns not involved.

to divide syphilitics into two classes: those with manifest cutaneous lesions, and those with absent or mild skin lesions and meningeal involvement, which division is too arbitrary for many cases with severe cutaneous lesions as well as those which have been treated early later develop disease of the nervous system. The observation of patients over long periods of time has shown that a low-grade meningitis may exist for years without producing obtrusive nervous symptoms. Such lesions are comparable to the superficial lingual and palmar syphilides, which persist for years, produce little inconvenience, and are refractory to treatment. There has been a good deal of speculation as to whether the spirochetes producing lesions in the central nervous system are the remains of

those deposited during the spirochetemia or whether they later reach the nervous system from another focus. Head's work is perhaps suggestive. In seeking to explain the more frequent involvement of some areas in root affections over others he found that the roots most commonly subjected to irritation were those in connection by their visceral afferent fibers with certain organs known to be the seat of active spirochetosis in syphilis. Thus the second and third cervical contain afferent paths from the tonsil; the first, second, third, and fourth thoracic from the aorta, while those from the seventh thoracic to the first lumbar, the most frequently involved, carry afferent paths from the liver, kidney,

FIG. 6.—Degenerated posterior nerve root in tabes. Posterior columns involved.

suprarenal, and testicle, organs which are the sites of election of the parasite. Orr and Rows have shown in their investigations on the lymphogenous infection of the nervous system that organisms and their toxins travel along the perineural lymphatic space which surrounds every spinal nerve and extends along the roots to the pia mater. These spaces are not only in connection with the pia, but through the latter in communication with the adventitial lymph spaces of the perforating vessels. The rôle of these channels as distributors is therefore quite obvious.

The sharp distinction formerly drawn by clinicians and laboratory workers between cerebrospinal syphilis and parasyphilis is no longer tenable. Gradually the barrier has given way until we have come to regard these conditions as identical from an etiological

stand-point, though differing in reaction, which difference depends on localization and the tissue involved. By cerebrospinal syphilis

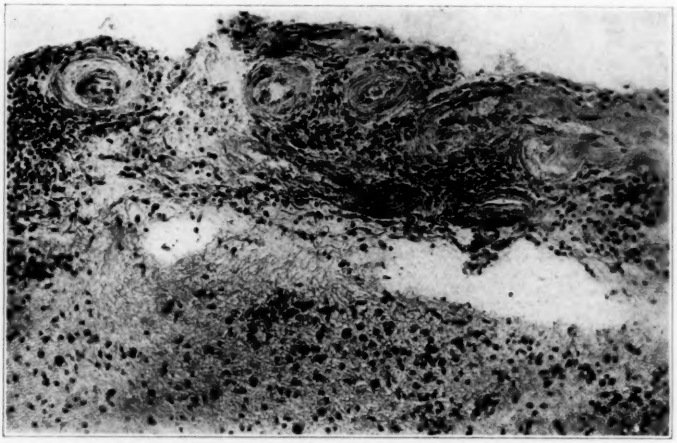

FIG. 7.—Syphilitic meningitis, showing various stages of obliterating endarteritis.

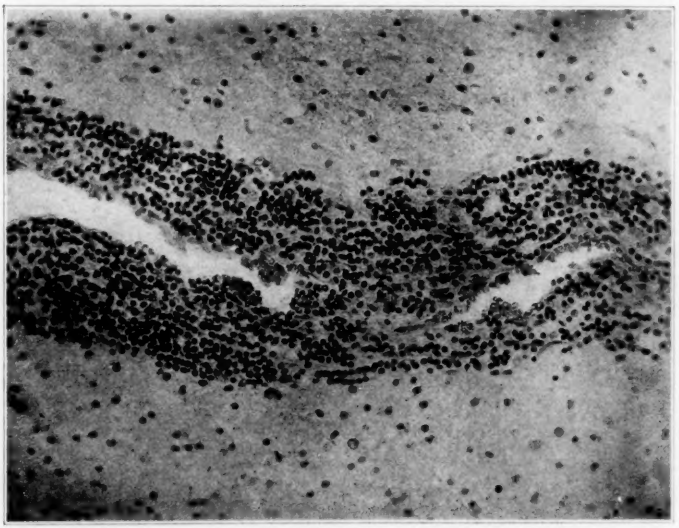

FIG. 8.—Mantling infiltration of lymphocytes and plasma cells about pial vessel in brain cortex.

we understand the exudative, vascular, and gummatous processes which involve the coverings of the nervous system and the blood-vessels within them (Figs. 7, 8, 9 and 10). These processes in the

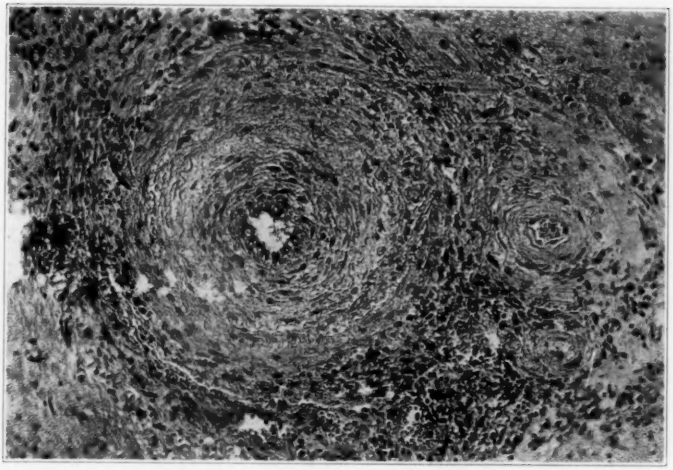

FIG. 9.—Heubner type of obliterating endarteritis in syphilitic meningitis.

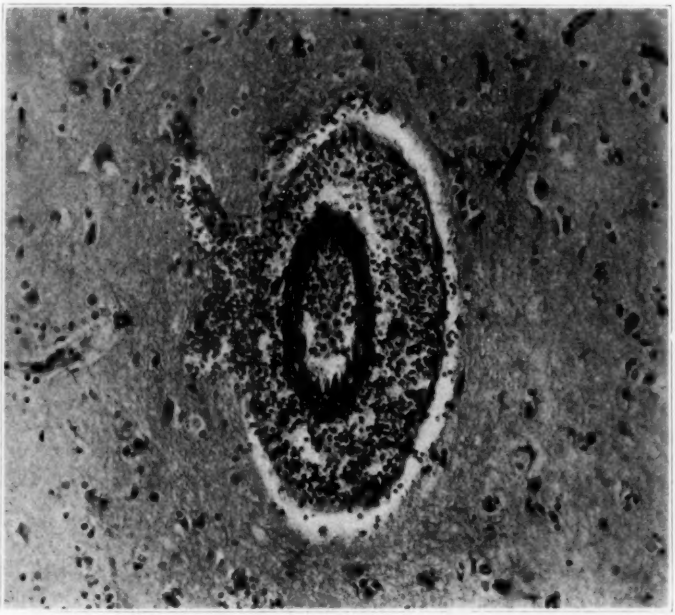

FIG. 10.—Small vessel in cortex of the brain, showing infiltration of perivascular spaces with lymphocytes and plasma cells.

great majority of cases remain superficial, but in some cases extend into the essential nervous structures along the pial or advential sheaths of the vessels, and give rise to the borderline cases of tabes and paresis.

It is proposed by Head and Fearnsides to divide luetic disease of the central nervous system into syphilis meningovascularis and syphilis centralis, the latter including all those cases where degeneration of nerve tracts or nuclei shows that the lesion must lie within the structure of the nervous system itself. As meningitis and endarteritis, however, are common to all these pathological states, this classification does not seem to the writer a tenable one.

What is the nature of paresis and tabes? In paresis there is a combined meningitis and encephalitis with a typical infiltration of lymphocytes and plasma cells in the adventitial lymph spaces (Figs. 11 and 12), the secondary degenerative changes probably depending on the primary vascular disease. Likewise we have a meningitis in tabes, but it is easier to comprehend the pathological condition and manner of invasion in paresis than the tract degeneration in the cord. The view that the genesis of both affections lies in a chronic meningitis now has a pretty wide acceptance. In tabes, Nonne believes it leads to disease of the roots and secondarily of the posterior columns. Nageotte was the first, in 1894, to describe a low-grade meningitis at the junction of the anterior and posterior roots on the proximal side of the ganglion, and in addition a neuritis, as shown by an inflammatory condition in the perineurium and a perivascular infiltration of plasma cells and lymphocytes in the posterior roots. This was confirmed by Dinkler, Dejerine, and others, but their views were not generally accepted, as the findings were interpreted as a combination. Again, in 1906, Schröder showed that collections of lymphocytes and plasma cells occur in the lymph spaces of the vessels in paresis and tabes, and that in the latter they are found not only in the pia and connective tissue about the vessels in the peripheral parts of the cord, but in the intramedullary portion of the columns as well.

Stargardt's findings in optic neuritis also have an important bearing. In a number of cases of tabes and paresis he found a true inflammation of the sheath and endoneurium. He also described an active inflammatory process in the joint structures of tabetic arthropathy, as evidenced by plasma cells and lymphocytes, with endarteritis of the small vessels. Steiner's studies on peripheral nerves in tabes and paresis also brought him to the conclusion that the process is an inflammatory one. The older view of a primary neuron degeneration in the light of present evidence would seem to have to be abandoned.

According to McIntosh, Fildes, Head, and Fearnsides, parasyphilis "depends upon an anaphylactic reaction in the tissues of the central nervous system which have been rendered hypersensi-

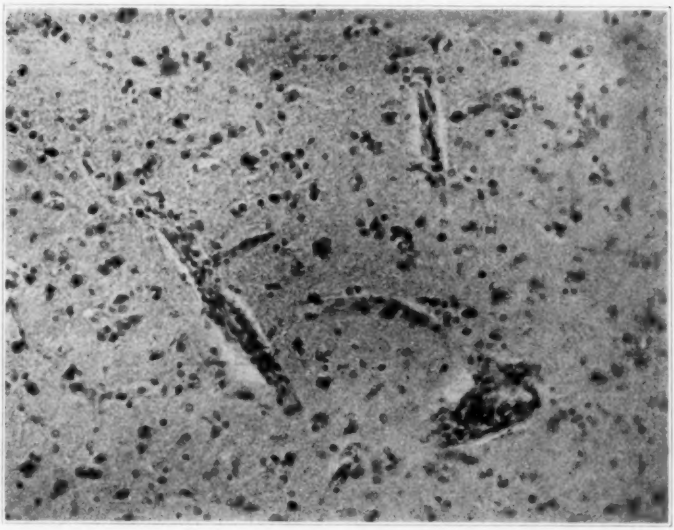

FIG. 11.—Showing the characteristic picture of paresis, with plasma-cell infiltration.

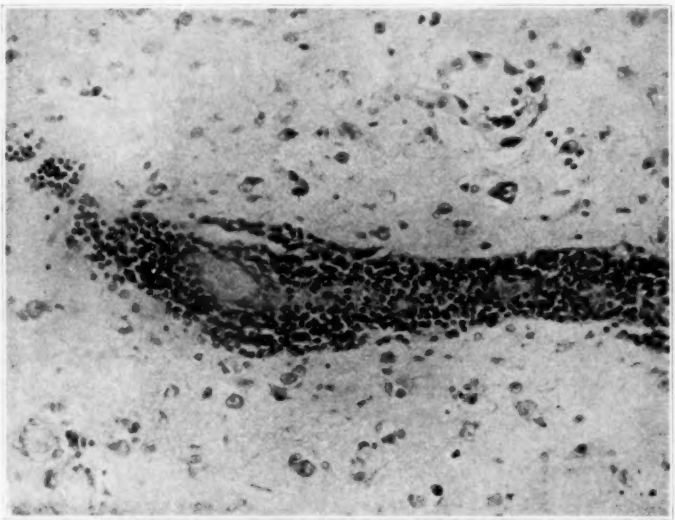

FIG. 12.—Paresis, showing the grouping of lymphocytes and plasma-cells about small vessels in cerebral cortex.

tive in accordance with their peculiar lymphatic distribution." Since it has been shown by Marie and Guillain, Orr and Rows, and others that the posterior columns are in direct lymphatic communication with the posterior roots, the aforementioned authors have evolved the theory that sensitization takes place during the secondary period by the spirochetes or their toxins ascending the afferent peripheral nerves. When spirochetes again become active in the posterior columns a violent reaction may ensue, injuring the nerve fibers and producing proliferation of the neuroglia and wandering cells. The injury of the nerve fibers will lead to degeneration, which will continue as far as the reflexion of the neurilemma. In the same way the cerebrum or isolated groups of cells in the anterior horns or other groups of fibers or cells alone or in combination may be affected, the particular region involved determining the clinical picture. Noguchi had previously shown by animal experiments that sensitization may be necessary before spirochetes can infect the brain. In both rabbits and monkeys he obtained negative results when the organisms were inoculated directly into the brain. He therefore injected rabbits with living and dead spirochetes intravenously, and after five months inoculated them subdurally with a particle of a scrotal syphiloma rich in spirochetes. They all remained well for two months, then became emaciated, and showed a slightly ataxic and spastic gait. The symptoms continued to increase, and after five months the animals were no longer able to jump. Microscopically some of these animals showed identical changes, with paresis, but the nerve cells were intact. In three an exudative meningitis was found and in one a unilateral atrophy of the frontal lobe. The control animals without previous sensitization remained well.

Analogies are frequently drawn between tabes and paresis and sleeping sickness. Spielmeyer, as the result of extensive investigations, came to the conclusion that in incipient cases the diagnosis between paresis and trypanosomiasis is not possible. He was able to produce in dogs with Trypanosma brucei an involvement of the central nervous system which was like human tabes. After nine to ten weeks the process was found in the posterior roots with beginning extension to the posterior columns, sensory trigeminus, and optic nerve. In trypanosomiasis, however, the central nervous system rarely escapes, whereas in syphilis only 1 or 2 per cent. develop tabes and 4 to 5 per cent. paresis.

Conclusions: Clinical observation and experimental work have shown that no true immunity exists in syphilis, but that an anergy develops during the first incubation period and is complete at the time of the general eruption. This refractory state usually persists as long as the body harbors spirochetes, and when it disappears, with the cure of the disease, the patient is again in a receptive state.

In the transmission of syphilis to the offspring the theory of spermatic infection has been abandoned in favor of placental infection, as the majority of mothers of congenitally syphilitic children have a positive Wassermann or show spirochetes in the intervillous spaces and maternal portion of the placenta.

The histopathology of syphilis is a uniform one. In all stages and in all organs the lesion begins in the perivascular lymph spaces as a lymphocytic and plasma-cell infiltration. The distribution of secondary lesions, according to Ehrmann, is due to a branching of the vascular stems. In the tertiary stage the ulcerative and destructive character of the lesions finds its explanation in a changed tissue reaction, the Umstimmung of Neisser, or allergy, in the sense of an increased susceptibility to the action of the organisms.

Syphilis produces a characteristic type of aortitis and is very common in individuals who have had the infection. It may be the only lesion present in so-called latent lues with a persistent positive Wassermann, and emphasizes the importance of examining all such patients for possible cardiovascular involvement. It is a frequent concomitant of paresis and tabes, especially the rudimentary form, occurring in about 80 per cent. of parasyphilitics.

Infection of the nervous system probably takes place during the secondary stage. A low-grade meningitis may exist for years or the spirochetes may remain quiescent for years until called into activity. In paresis a mantling infiltration of lymphocytes and plasma cells is found in the adventitial lymph spaces of the meninges and encephalon. From its pathological anatomy, which has been studied in all stages, it is much easier to comprehend this condition than the tract degeneration in tabes, as tabetics seldom die during the early period of the affection. The few pathological examinations which have been made, reveal, however, changes in the meninges about the posterior roots between the ganglion and the cord. It is not so difficult to understand how an infiltration in this region by pressure could produce degeneration of the afferent fibers extending to the posterior columns and leading to an ascending tract degeneration following the well-known law that a destruction of the neuron is followed by degeneration along its distribution. This explanation is a much more plausible one than a primary degeneration without inflammatory manifestations.

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THE VALUE OF CERTAIN TESTS FOR DIAGNOSIS AND PROGNOSIS IN CHRONIC NEPHRITIS.

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Numerous tests have been devised from time to time in order to make an early diagnosis or prognosis in chronic nephritis. Also by a study of the responses to certain tests attempts have been made in recent years to classify the different types of chronic nephritis.

Of these different tests the examination of the urine for albumin and casts and the determination of the blood-pressure have been used pretty generally, especially for making a diagnosis of renal trouble. Recently, Rowntree and Geraghty[1] devised the now well-known test which depends upon the elimination of phenolsulphone-

[1] Jour. Pharm. and Exp. Ther., 1910, i, 579.

phthalein in the urine. Since its origin a considerable amount of work has been done on this test in regard to its ability to demonstrate chronic nephritis in the early stages or to make an accurate prognosis of the eventual outcome.

More recently Folin and Denis[2] have devised a technique for determining the non-protein nitrogen content of the blood which has given a fresh stimulus to this well-known method for studying renal disease and made it practical for clinical use. As a result, reports are coming from several clinics on the value of the non-protein nitrogen content of the blood in diagnosis, prognosis, and classification of chronic nephritis.

For years the study of the kidneys' ability to excrete sodium chloride and various forms of nitrogen has been carried on. Usually these studies have been made by a quantitative determination of the intake in the food and the output in the urine of sodium chloride and nitrogen. It has been found that the ability of the individual to put out in the urine salt and nitrogen varies in different types and stages of nephritis. Widal,[3] Müller,[4] Monakow,[5] and others have attempted to arrange the cases into groups according to the retention of one or the other of these substances.

In one group these authors place the cases with salt retention and normal nitrogen elimination. In another, the cases with nitrogen retention but fairly good salt elimination. Both of these groups present clinical symptoms according to these authors which are characteristic. Many of the cases, however, are a combination of the two types.

In order to test more rapidly the ability of the individual to excrete salt in the urine, Schlayer[6] suggested the addition of 10 grams of sodium chloride to the diet at one dose after the patient had reached a salt equilibrium by being on a known diet for several days. In a normal individual this added salt should appear in the urine in twenty-four hours according to some authors, or at most in forty-eight hours. Monakow[7] devised a similar test to show the ability to put out nitrogen, which consisted in giving 20 grams of urea at one dose under similar circumstances. The nitrogen content of this urea, approximately 10 grams, should also be excreted in twenty-four to forty-eight hours by a normal individual.

Of course, it is possible that an individual might excrete the full amount of salt and nitrogen contained in the daily diet and yet fail to put out properly the excess of these substances given at one time. Doll and Siebeck[8] have emphasized this point in some recent work. However, experience has shown that these two tests offer

[2] Jour. Biol. Chem., 1912, xi, 527.
[3] La Semaine Médicale, 1905, xxv, 313.
[4] Verhandl. der Deutsch. path. Gesellschaft, Moran, 1905.
[5] Deutsch. Archiv. f. klin. Med., 1914, cxvi, 1.
[6] Ibid., 1910–11, ci, 333.
[7] Ibid., 1911, cii, 248.
[8] Ibid., 1914, cxvi, 549.

a fairly good guide to the ability of the kidneys to take care of salt and nitrogen, and they have been used in recent years quite extensively for this purpose.

Recently, Ambard and Weil[9] have offered a method for determining salt and urea retention which consists in finding the blood content of these substances at a given time and their output in the urine at the corresponding time. It is hoped in this way the salt and nitrogen retention may be more readily determined.

Many other tests have been suggested for renal study, but those mentioned above seem to have received most attention in recent literature. Foremost among the workers on nephritis is Schlayer, who, with his assistants, has tried out many tests experimentally and clinically, including the lactose test of Voit[10] and the potassium iodide test of Duckworth.[11] More recently Hedinger and Schlayer[12] have been studying the work of the kidney by means of test meals, which are given for several days. The response of the kidneys at different periods of the day is carefully studied, and seems to be of both diagnostic and prognostic importance.

Since the opening of the Peter Bent Brigham Hospital the cases suspected of having chronic nephritis have been studied by a variety of tests. Up to the present time most attention has been paid to the blood-pressure, urinary examinations, phenolsulphonephthalein excretion, non-protein nitrogen content of the blood, and the ability to excrete in the urine added amounts of salt and urea given by the mouth. At the present time studies are being made on the cases of chronic nephritis by means of Schlayer's test diets, with modifications, and the Ambard and Weil method for determining salt and urea retention.

A sufficient number of cases of chronic nephritis have been studied by all of the six tests mentioned above to make a comparison of them of interest in order to decide on the value of these different tests for diagnosis, prognosis, and the purpose of classification. In all, over 100 cases diagnosed eventually as chronic nephritis have been studied by most of these tests. In only 40, however, have the tests been completed in all their details, and therefore this report will be limited to these 40 cases. It may be said, however, that the other cases in which some one or part of a test was lacking, apparently responded to the tests similarly to the forty reported.

The data collected in the accompanying table was obtained from the medical records of the hospital, and represent results obtained by a number of men on the staff either in their routine work or in some special study. The entrance blood-pressure is recorded, as it became evident that the pressure in most cases in

[9] Jour. de phys. et de path. gen., 1912, xiv, 753.
[10] Deutsch. Arch. f. klin. Med., 1897, lviii, 545.
[11] Bartholomew's Hosp. Rep., 1867, iii, 216.
[12] Deutsch. Arch. f. klin. Med., 1914, cxiv, 120.

which it was elevated fell after rest in the hospital. This reading also is probably nearer to that which would be found on meeting the patient in practice.

In the report on the urine the general impression from several examinations was recorded; for it is so well known that a single examination of the urine may not show albumin and casts which will be present on subsequent examinations.

The amount of non-protein nitrogen in the blood was determined by the method of Folin and Denis and the amount found on the first examination recorded; for in many of the cases attempts were made to change the amount by variations in the diet.

The phenolsulphonephthalein test has been done by the method originally suggested by Rowntree and Geraghty and the total excretion for two hours recorded. The first estimation after entrance was taken, and therefore it must be borne in mind that if passive congestion of a severe grade were present the output may have been considerably lower for that reason.

For several days before giving the extra amounts of sodium chloride and urea the patients were placed on a known diet and their ability to put out salt and nitrogen recorded until the amount became practically constant. The amount of salt or nitrogen in excess of that excreted on the day preceding the dosage was recorded for the first and second twenty-four-hour periods following the dose. In some instances the amount excreted on one or the other day was less than that on the control day. In such instances a minus sign is placed before the figure.

In order to group the cases according to their response to these tests the excretion was considered normal if 8.5 grams of the 10 grams of added salt or nitrogen were put out in the forty-eight hours. It was considered a slight retention if between 4.5 grams and 8.5 grams were excreted. If less than 4.5 grams were put out in the forty-eight hours the retention was considered marked.

Clinically the cases in the accompanying table varied from the edematous patients with normal or slightly elevated blood-pressures and considerable evidence of active renal disturbance without uremic symptoms, to the cases with high pressure, shortness of breath, marked uremic phenomena, pronounced eye-ground changes, and with or without edema.

The severest cases of nephritis are not included in this list because it was not considered advisable to give them added salt and urea, and because frequently it was impossible to feed them with enough regularity to find their normal elimination. It is interesting to note that cases with the same clinical course frequently showed at autopsy a form of chronic nephritis quite different from each other.

Of these 40 cases representing different types and grades of chronic nephritis, 37 showed a systolic blood-pressure of 150 or above, which is usually considered as abnormal. In 3 cases the pressure

Hospital No.	Systolic pressure.	Urine.		Blood nitrogen per 100 c.c.	Per cent. phthalein in 2 hours.	Grams of NaCl above control.		Grams of nitrogen above control.		Complications.
		Albumin.	Casts.			1st day.	2d day.	1st day.	2d day.	
1443	225	+	Rare	27.2 mgs.	33	5.3	−0.3	9.6	0.0	Cardiac; no edema.
1358	145	+	+	46.0 mgs.	6	4.8	0.9	1.0	−1.2	None; no edema.
1340	225	+	+	35.2 mgs.	38	1.2	3.2	3.0	−0.8	None; no edema.
1023	258	+	+	36.0 mgs.	30	1.0	1.0	3.0	1.0	None; edema.
1197	225	+	+	39.0 mgs.	54	0.0	2.0	2.0	2.0	None; no edema.
1139	210	+	Rare	38.2 mgs.	51	3.5	3.0	4.0	1.5	None; no edema.
1170	230	+	+	34.2 mgs.	50	6.0	2.0	4.0	2.0	Cerebral; no edema; arteriosclerosis.
1154	258	+	+	30.9 mgs.	45	−2.9	−1.8	12.0	2.2	None; edema.
1178	128	+	+	20.0 mgs.	54	1.5	2.0	2.0	−0.5	Cirrhosis of liver; edema; arteriosclerosis.
1072	200	+	+	31.0 mgs.	51	2.0	1.0	4.0	4.0	Arteriosclerosis; no edema.
1365	185	+	+	36.5 mgs.	33	2.0	−0.1	7.2	3.7	Cardiac; edema.
1490	270	+	+	26.8 mgs.	34	−0.3	−3.8	5.4	2.3	Cardiac; no edema.
974	190	+	+	54.1 mgs.	25	1.0	0.0	8.0	8.0	None; no edema.
986	180	Rare	Rare	25.9 mgs.	36	2.6	−0.9	5.0	4.0	Cardiac; edema.
918	245	+	+	70.9 mgs.	14	0.5	−1.5	0.5	−6.0	None; edema.
1056	218	+	+	78.9 mgs.	0	1.0	−1.0	−2.0	3.0	Arteriosclerosis; no edema.
1075	192	+	+	23.8 mgs.	55	−1.0	3.0	8.0	1.15	None; edema.
1885	154	+	+	39.0 mgs.	24	.0	2.1	2.0	2.0	Cardiac; edema.
1918	254	+	+	31.0 mgs.	49	.0	2.5	3.0	2.0	None; no edema.
1948	220	+	0	25.0 mgs.	65	4.5	5.5	9.0	−1.5	Cardiac; no edema.
2077	255	+	+	23.0 mgs.	52	2.0	−2.0	8.0	2.0	Myocarditis; no edema.
2074	164	+	+	40.0 mgs.	18	1.5	1.5	1.0	1.0	None; no edema.
1898	200	+	+	32.0 mgs.	43	2.5	1.0	6.0	9.0	Cardiac; edema.
1696	170	+	+	16.5 mgs.	54	0.0	3.0	4.0	−2.0	Cardiac; no edema.
1814	186	+	0	33.0 mgs.	42	0.0	−3.5	5.0	4.0	Cardiac; edema.
1661	190	+	+	38.0 mgs.	42	2.0	1.8	9.0	4.0	Diabetes; no edema; myocarditis.
1459	220	+	+	21.3 mgs.	48	0.0	3.0	3.0	1.0	None; edema.
1738	190	+	Rare	25.0 mgs.	50	3.0	1.5	8.0	2.0	None; no edema.
1804	260	+	Rare	33.0 mgs.	59	0.0	2.5	6.5	−1.0	Myocarditis; no edema.
1754	122	+	+	36.0 mgs.	28	−0.5	0.5	0.5	−0.5	None; edema.
1624	150	+	+	40.0 mgs.	28	1.0	2.0	6.0	2.0	None; edema.
1608	230	+	0	76.2 mgs.	15	−4.0	−2.0	2.0	0.0	Lead arteriosclerosis; no edema.
1821	188	+	+	33.0 mgs.	18	4.5	1.0	0.0	0.0	None; no edema.
1760	250	+	+	28.0 mgs.	30	−0.5	0.0	1.0	−1.0	None; no edema.
624	220	Rare	Rare	25.4 mgs.	45	−2.5	−4.7	3.9	3.0	Arteriosclerosis; edema.
684	210	+	Rare	25.0 mgs.	65	3.2	4.2	7.0	4.0	None; no edema.
762	180	+	+	50.0 mgs.	35	1.0	−0.5	4.0	1.0	None; edema.
782	185	Rare	0	33.2 mgs.	58	2.0	5.0	9.0	1.8	Acute rheumatism; no edema.
817	212	Rare	Rare	31.8 mgs.	56	1.8	1.6	5.0	2.0	None; no edema.
548	190	+	Rare	23.2 mgs.	45	3.3	−0.1	10.0	3.0	Cardiac; no edema.

was apparently normal. It seems fair, therefore, to decide that an elevated blood-pressure occurs with sufficient frequency to be a good aid in diagnosis. In another work, Smillie and Frothingham[13] have shown that the height of the blood-pressure is not a definite guide to the severity of the nephritis. Although it tends to be slightly higher on an average in the severer cases, the individual variation is so marked that very little aid for prognosis can be obtained from it.

The 3 cases with normal blood-pressure did not fall into any one clinical group, and cases with quite different clinical signs showed an elevated blood-pressure. Therefore, it is evident that the blood-pressure determination is not of much value in regard to the clinical classification of chronic nephritis.

In 36 of the cases albumin was present in varying amounts in all or most of the examinations; in 4 it was present so infrequently that its presence might have been overlooked even after several tests; 27 cases showed casts most of the time, 9 only rarely, and 4 not at all. It is evident that albumin is almost as common a sign in chronic nephritis as a high blood-pressure, but that casts do not occur so frequently. On account of the presence of albumin and casts in other conditions than chronic nephritis the occurrence of them in the urine is not of sure diagnostic value, but it offers a good guide for further study, and few cases would be missed by these tests alone if more than one examination were made.

It is well known that some of the most severe cases bordering on uremia show little or no albumin or casts in the urine, so that for prognosis these tests are of practically no value.

The number and character of the casts, however, are of considerable value as a guide to the amount of renal destruction actually going on at a given time. On the other hand, a large amount of albumin may mean a considerable amount of active renal destruction, or it may simply show a leakage through the kidney of serum albumin. Cases of a similar clinical type, namely, those in younger people with considerable edema, usually show considerable albumin and many casts in the urine, but other clinical types of nephritis also at times show much albumin and many casts. Therefore, for the purpose of a clinical classification of chronic nephritis, the presence or amount of albumin and casts in the urine is not of much assistance.

Thirty mgm. or less per 100 c.c. of blood was considered the normal content of non-protein nitrogen for the blood. With this as a standard, 26 of the 40 cases showed an increase over the normal of non-protein nitrogen. In 14 cases the amount fell within the normal limits. It is evident, therefore, that cases which are recognized as chronic nephritis may have a normal non-protein nitrogen content in the blood. Thus, for an early diagnosis of chronic nephritis this

[13] Arch. Int. Med., 1915, xv, 204.

test is not of great value. On the other hand, in patients whose unconsciousness is due to uremia the non-protein nitrogen is always elevated in our experience, and, therefore, in this type of case the test is of considerable value in making a differential diagnosis. For prognosis this test is of considerable value. There seems to be a fairly direct relation between the severity of the nephritis and the amount of non-protein nitrogen in the blood as was shown in a study of these and other nephritis cases by Frothingham and Smillie.[14]

The cases in this series with the same clinical type of chronic nephritis varied from a normal amount to a marked elevation of the non-protein nitrogen content of the blood, also some of the cases of all the clinical types included showed an elevated and others a normal blood nitrogen. It was felt, therefore, that this test would be of little value in the classification of chronic nephritis.

Fifty per cent. or more of the phenolsulphonephthalein should be excreted under normal conditions in two hours. Of these 40 cases 26 showed a diminished 'phthalein excretion and 14 put out a normal amount. This series showed, therefore, what has been found repeatedly, that certain cases of chronic nephritis have, especially in the early stages, a normal 'phthalein excretion. Therefore, for diagnosis in the early stages of the disease this test is not reliable. Furthermore, the diminished 'phthalein excretion in some of the cases may have been due to passive congestion.

For prognosis the test is more valuable provided that passive congestion is ruled out. This is specially true in the cases in which the 'phthalein elimination is markedly diminished. In this class of cases other tests and the clinical findings usually point to a severe nephritis. Occasionally for some unexplained reason in the severe cases of chronic nephritis the 'phthalein output may be practically normal. In some at least of all the clinical types of chronic nephritis studied the 'phthalein elimination was lowered, and so for the purpose of classification of chronic nephritis this test is not of value.

Of the 40 cases only 1 showed a normal excretion of the extra sodium chlorine; 8 had what has been arbitrarily called a moderate retention of the added salt, and 31 were very markedly unable to excrete it. Apparently, therefore, disturbance in the ability to eliminate salt is a common occurrence in all types of chronic nephritis and may be considered a good diagnostic sign. For prognosis this test is not of much value, because the kidneys apparently lose the ability to excrete the added salt in appreciable amounts before the other tests suggest that the nephritis has become severe. Although other authors have attempted to group the cases of chronic nephritis somewhat in their relation to sodium chloride excretion, it was not possible to do so in this series, because practically all the cases, including a variety of clinical types, showed the inability to excrete it.

[14] Loc. cit.

Fifteen of the 40 cases excreted the added urea well, 9 fairly well, according to the set standard, and 16 showed a marked inability to excrete it. This test, therefore, can not be depended upon for making an early diagnosis. For prognosis the test is more useful, as in all but 3 of the 16 cases, which showed a marked retention, the other evidence pointed to a severe grade of nephritis.

This test has not been of value for classifying chronic nephritis, for in cases which are apparently of the same type the excretion of the urea varies considerably. In all but 3 of the 16 cases with marked urea retention the salt retention was also marked. In these 3 cases the salt retention was moderate. Therefore, although there were some cases with what might be termed pure salt retention, there were none in which there could be said to be a pure nitrogen retention.

Twenty-five of the 40 cases showed edema at entrance. Of course, it cannot be definitely determined in how many of these cases the edema was due to cardiac disturbance. A list of the important complications to the chronic nephritis is also added in the table.

From this study it seems fair to conclude that the blood-pressure determination, repeated urinary examinations, and a study of the ability of the kidney to excrete extra sodium chloride are the most reliable tests for making an early diagnosis of chronic nephritis.

For prognosis in chronic nephritis the determination of the non-protein nitrogen in the blood, the excretion of phenolsulphone-phthalein in the urine, and the ability to excrete extra nitrogen in the urine are the most useful tests.

By means of these tests it is not possible to group the cases of chronic nephritis in relation to their clinical appearance. Further study on the relation of these tests to the pathological lesions in the kidney is being carried on.

PRACTICAL IMPORTANCE OF EXAMINATION OF STOOLS IN INFANTS.

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The subject of infant feeding involves many problems. Every physician of experience meets with cases that baffle his skill and try his patience, although great progress has been made during the last few years. Percentage feeding as developed by the late

Professor Rotch has certainly led to a more careful study of the problem and has helped in lifting it out of the chaotic state. The estimation of the caloric value of food is another step in advance, however. As the caloric needs of an infant may be met with a diet lacking in important food elements, it cannot in itself be considered a system. It is, however, of practical value in checking up any cases of overfeeding or underfeeding.

Fortunately many infants will do well on any reasonable modification of milk. The feeding of the infant may be considered satisfactory if it is comfortable, if there is a steady gain in weight and increasing strength, and if the gain in weight is properly balanced. Every physician has observed infants with a feeble musculature, soft bones, and often evidence of rickets, make a steady gain on condensed milk and water. Such a gain is not satisfactory. If in the ordinary case the stools appear normal, that is, a proper color, smooth and free from offensive odor, while the child is gaining in weight, then such a case requires no further consideration. On the other hand, there are cases where the examination of the stool is a valuable practical aid. In these cases mere inspection does not give sufficient information. One of us (Dr. J. Clyde Moore) made 125 examinations in the manner to be described. We feel that as a result of these examinations we have been able to treat our cases more intelligently and to obtain better results. In all of our feeding cases we use the following plan of obtaining the necessary facts: First we make an analysis of the milk, human or cow's milk. We examine for specific gravity, reaction, fat, carbohydrates, and proteid. Occasionally we make bacteriological tests when it seems desirable. The Babcock method is used for determination of the fat in both human and cow's milk. For the human milk we use a Babcock tube specially designed for the medical centrifuge. On account of the smallness in quantity of milk we always make four tests and take the average. For sugar we precipitate the lactalbumin and casein by acetic acid and heat and titrate with Fehling's solution. For estimation of proteids in cow's milk we use the formula of Bowditch and Bosworth. The fat is determined by the Babcock method, the specific gravity is taken with the ordinary lactometer and corrected for temperature, and the sugars and proteids calculated according to the following:

1. Total solids: $L/4 + (1.2 \times F)$ = total solids.
2. Casein: $(F. - 3) \times 0.4 + 2.1$ = casein.
3. Total proteins = $(F - 3) \times 0.4 + 2.8$.
4. Sugars: total solids — (F + total proteid + 0.9.)

L = reading of Quevenne lactometer.

F = per cent. fat as determined by Babcock method.

This gives a formula exact enough for clinical purposes. The next point of consideration is the baby itself as to age, previous

feeding, weight curve, energy quotient, and clinical symptoms, such as colic, vomiting, regurgitation, and number and character of stools. The latter often gives important information, and should be carefully followed in every case. The methods used by us are as follows:

The stool is collected on the diaper or square of gauze and then put in a small vaselin jar with a screw top, so as to prevent drying before examination. The following outline is used in the examination: Number of stools; color; reaction; odor; consistency; blood; mucus; curds; neutral fats; fatty acids; soaps; total fat; reaction to Lugol's solution; Gram-negative bacilli; Gram-positive bacilli.

The reaction is determined by moist litmus paper, being careful to take the specimen from the centre of the stool. The mucus is determined macroscopically, and if in doubt, by staining with iodin solution. Partially digested starch, which is sometimes confused with mucus, stains bluish pink, while mucus is unaffected. In one case thought to contain mucus, examination revealed starch. The use of a dextrinized gruel instead of cereal gruel caused complete disappearance of apparent mucus from the stool. Curds are always determined macroscopically. The simplest method for determination of the character of the curds is to treat them with formalin, the casein curds hardening in this while the fat curds are not affected. Fat curds will float in water. Casein curds sink. For some time there has been contention over the composition of curds. Meyer and Leopold have contended that all curds are really fat curds, but Talbot, Morse, and others have proved conclusively, by biological and chemical experiments, that the large, tough, citron-colored curds occasionally found in infant's stools are casein curds. The small flocculent curds found very often are fatty acid or neutral fat curds. The significance of these curds will be discussed later.

For estimation of fats we use the methods advocated by Morse and Talbot and by Cowie and Hubbard. The former is of value in giving a quick, general idea of fat digestion. The method is as follows: From a thoroughly mixed stool a small fragment is taken and put on a slide, a drop of the saturated solution of Sudan III is added and thoroughly mixed in; cover with cover-glass and examine under low power with No. 1 objective; fat appears as bright-red droplets scattered through the field; fatty acids also stain, but are of an orange hue; soaps do not stain. To another fragment a drop of dilute carbofuchsin is added. This does not stain the neutral fat, but does stain fatty acids and soap splinters. A comparison of this slide with the previous one gives a rough estimate of the neutral fats and fatty acids and soaps. To the Sudan III slide then a drop of glacial acetic acid is added and the slide heated until bubbles begin to appear under the cover-glass. This changes all of the fat into the fatty acids which show up as red-

stained droplets. If there is a large increase in the number of drops after adding the acetic acid it is known that a large amount of the fat has been present as soaps. A comparison of the number of drops with the residue on the slide gives a rough estimate of the total fat. Dr. Talbot has devised a scheme for more accurate estimating by counting the drops in the field. Since, however, this is simply a rough, comparative method, and as we have found that different fields on the same slide differ so materially, we conclude that the general appearance of the slide is sufficient without counting the drops in any certain field. Much information can be obtained by this simple method of examination, which is very satisfactory in our work. For a more accurate study of the total fat in the stool we have recently been using the method suggested by Cowie and Hubbard, of the University of Michigan. One-half gram of moist stool or 0.25 gram of pulverized stool is carefully weighed out and rubbed up in a beaker or thin-lipped mortar with 20 c.c. of warm water and then transferred to a Babcock milk bottle graduated in fiftieths. The water is added little by little to the specimen so that the entire portion can be transferred to the milk bottle with the first 10 or 15 c.c. of water, using the last 5 or 10 c.c. to wash the mortar and pestle. The sample is thoroughly mixed and 17.5 c.c. of H_2SO_4 (1.84) added slowly. Mix by shaking vigorously and then add 1 c.c. of amylic alcohol. Counterpoise and centrifuge for three minutes at a rate of about 1500 revolutions to the minute. Add hot water to bring the fat into the graduated stem of the bottle; centrifuge for one minute and then read with bottle immersed in hot water. If 0.25 gram of stool has been used, multiply percentage on stem of tube occupied by fat column by factor 7.2; if 0.5 gram sample of stool is used, multiply by the factor 3.6; the result is the percentage of fat in sample examined. To estimate total of fat in twenty-four hours, weigh each stool as passed and multiply by percentage obtained in sample examined. This work can easily be done within fifteen to twenty minutes. The apparatus necessary is an ordinary prescription balance, a 2 bottle Babcock hand centrifuge, and Babcock skimmed milk bottles. The latter are graduated in hundredths instead of fiftieths, but the same result is obtained.

Sugars. The examination of sugars is limited to the examination for lactic acid. Uffelman's test is fairly satisfactory. Clinically, however, the odor and reaction of the stool gives all information necessary. Babies with excess of sugar have distended abdomens due to excess of gas.

Proteids. This is limited to examination macroscopically for casein curds.

Bacteriological Examination. In this work we have only tried to determine the predominance of either Gram-negative or Gram-positive bacteria. No cultural methods are used except

for particular study of some case. Sterilized milk is the culture most frequently used. We have followed the methods outlined by Vincent, of London, in this work.

SIGNIFICANCE OF DATA. *Color.* The normal breast milk stool is golden yellow, sometimes becoming greenish in tinge on standing. The color of the stool of artificially fed babies depends upon the food given and condition of digestion. The normal stool is a light yellow. Malt feedings give brown stools. Condensed milk light yellow. Skimmed milk, very pale stools. Excessive soap whitish stools. In various infections stools may be green. The green color of the stool, however, is not of so much importance as usually considered. Always ascertain if the stool was green when passed or changed in color on exposure to air. The color is due to the change of bilirubin to biliverdin, and may be caused by excessive acidity or alkalinity of intestinal contents or by the presence of some oxidizing ferment. A greenish color may also be due to the Bacillus pyocyaneus. This latter color disappears when the stool is treated with nitric acid, while that due to biliverdin gives the characteristic bile reaction. A gray stool may be due to the absence of bile, as in congenital obliteration of the bile ducts or certain diseases of the duodenum or biliary tract, or it may be due to soap. Various drugs may color the stool. Blood may color the stool black.

Reaction. A highly acid stool is usually due to relative excess of carbohydrate. We also get a very acid stool with fatty acid. A relative excess of proteid gives an alkaline stool. Soap stools are alkaline.

Odor. The normal stool has a slight sweetish odor. Stools with excessive putrefaction, as when there is a relative excess of proteid, have a musty or cheesy odor, sometimes taking on a distinctly fecal type. When there is fever the odor is that of decayed egg. The fatty acid stool or that due to excessive carbohydrates gives the sour odor of butyric or lactic acid.

Consistency. The normal stool of a breast-fed baby is thin and mushy. That of a baby on cow's milk is usually thicker and more pasty. The stool with excessive neutral fat or fatty acid is usually soft and oily, with excessive soap hard, or dry and crumbly, with excessive carbohydrate varies from mushy, foamy type to thin and watery. Excessive proteid seems to make but little difference in the consistency of the stool unless causing a diarrhea. Occasionally foamy stools are found with excessive proteid. Malt soup nearly always gives a salve-like stool of a characteristic brown color. A watery stool indicates either some irritable condition of intestine which causes its contents to be hurried through without allowing absorption of water, or else the presence of some substance which by osmosis draws the water from the vascular system into the intestines. The associated history and clinical symptoms usually reveal the nature of this substance.

Blood. Blood is occasionally found in infant stools. Black blood, macroscopically visible or as occult blood, in a marasmic baby in nearly every case points toward duodenal ulcer or blood swallowed from a fissured nipple. An infant breast fed, aged five months, gave us serious concern because of blood in the stool, until it was discovered that the infant was getting the blood from the mother's nipple. Fresh blood is often caused by a fissure in anus or lesion in colon or by a proctitis. In cases with fresh blood, careful inspection of rectum should be made.

Mucus. Mucus always indicates some irritation of the intestinal tract, either chemical, bacteriological, or mechanical, as often noticed in cases of dry constipation.

Curds. Small, flaky fat curds in the stool of a newborn breast-fed baby have no significance. We do not consider them of any marked significance even later in infancy unless accompanied by other clinical signs of an indigestion. The large fat curds occasionally encountered indicate some disturbance of fat digestion and absorption, and may be due to excessive fat in the feeding, lowered tolerance for fat, or a proteid or carbohydrate high enough to cause irritation of intestine and thus interfere with fat absorption. Which of these factors come into play must be decided after a study of the diet in the individual case.

The casein curd when accompanied by clinical signs of disturbed digestion, such as colic, either diarrhea or constipation, restlessness, etc., usually point to poor proteid digestion. The casein curd, however, may appear in the stool and be of no significance. Heating the milk or the addition of some protective colloid, such as barley water or sodium citrate by preventing the firm coagulation of the milk in the stomach, stops the appearance of curds in the stool. The value of sodium citrate was strikingly proved in two cases, 1 grain to the ounce of milk preventing curds.

Neutral Fats. The excess of neutral fat as shown by the staining method indicates either a lowered tolerance for fats, that is an inability to digest and absorb normal amount of fat, or it indicates an excess of fat in the food.

Fatty Acids and Soaps. An excess of these indicates that the neutral fat has been broken up by the digestive processes, but that for some reason or other there has been a failure of absorption. This condition should always lead to suspicion of tuberculosis. There are several theories advanced as to the reason for soap stools. Meyer, Stolte, Usuki, and others have shown that the three requisites for a soap stool are a moderate amount of fat, casein, and calcium in considerable quantity, and the absence of sufficient carbohydrate. A case under our observation recently showed this very clearly. The food was, approximately, fat 2 per cent., sugar 2 per cent. proteid 1.7 per cent., with about 5 per cent. of lime water. The stools were alternately of the foamy, putrefactive

type, and the hard, soap type. Addition of sufficient carbohydrate brought immediate change in the stool. Excessive fatty acid in intestinal contents often produces a diarrheal stool. Accompanying this is a marked loss of sodium and potassium, and a relative acidosis is developed. We believe this is a practical point worthy of consideration in cases of cyclic vomiting. In the soap stool mentioned above there is a positive sodium and potassium balance, but a negative calcium and magnesium balance.

Total Fat. So far we have only used the Cowie and Hubbard method in observing cases in which we were trying to increase the fat tolerance. We occasionally find cases which seem unable to digest the smallest quantities of fat. These cases may, however, have their fat tolerance gradually increased by carefully increasing the fat content of their food as they are able to digest it. In these cases an increase of the total fat in the stool, especially if persistent and rising, is an indication for lowering the fat percentage of the food. We find fat tolerance is usually reëstablished by withdrawing fat for a few days then slowly increasing.

The Reaction to Lugol's Solution. The presence of blue-staining particles means undigested starch. It is very common in cases on barley water to find partially digested vegetable cells staining blue with the iodin solution. Certain bacteria accompanying disturbances of carbohydrate digestion stain blue with Lugol's solution.

Bacteriological Examination. As mentioned above, we only determine the preponderance of the colon or lactic type, that is, the Gram-negative or Gram-positive type. A marked preponderance of the colon type indicates a change from normal fermentation to putrefaction. This is shown particularly when the colon bacilli take the methylene blue stain poorly. Vincent says that this indicates a change in the colon bacillus from fermentative to proteolytic type. We have seen this type very markedly in two recent cases of apparent colon toxemia. We wish to emphasize that the examination of the stool is a very important point in feeding cases, and should be made in all cases of bottle-fed infants. There should be repeated examinations of both milk and stools during the whole course. In this way the feeding can be made definite and well balanced. It is, however, only one means of watching the case, and should not be relied on to the exclusion of the weight curve and energy quotient.

Conclusion. Chemical and microscopic examination of stools has passed the experimental or laboratory stage. In any well-worked-up case the procedure ranks with blood counts and urinalysis in importance. Indeed, in infants with intestinal indigestion, it is the only accurate method of determining the food element that causes the disturbance. The conclusions drawn from the examination of the stools give information of practical value.

IMMUNITY IN TUBERCULOSIS: WITH SPECIAL REFERENCE TO RACIAL AND CLINICAL MANIFESTATIONS.[1]

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Nine years ago Professor Theobald Smith[2] delivered an address before this body on the subject of tuberculosis, with especial reference to the parasitic properties of the tubercle bacilli. He gave a most illuminating view of the bacillus from the biologist's point of view as well as a working theory of the reciprocal action of the tissues and parasite.

I refer to his hypothesis that the bacillus forms a protective envelope or capsule which permits it to retain vitality in a latent focus. He further explained the mechanism of infection and immunity, and presented the problem for clinical medicine as developed up to that time.

I fear that my selection for a similar task is inadequate; certainly I am deeply conscious of the responsibility and honor in offering the Harvey Society this effort to supplement that of our most distinguished American worker in tuberculosis.

It appeared to me better suited and more useful at the present time to treat the subject of immunity in its clinical aspect, and, while discussing some of the recent laboratory researches, to take also a broad survey of tuberculosis from the racial and epidemiological view-point. We may in this way discover a proper attitude toward the complex problem of prevention and treatment of tuberculosis, a matter fraught with frequent misunderstandings and wide differences of opinion. Only by this combination of experimental and clinical experience have we any claim to judicious decisions. Too often we encounter confusion and perplexity in the face of the frequent contradictions met with in tuberculosis from the clinical side. The deceptions and fallacies of laboratory experiments have also led us astray to the discouragement of many. It must be admitted to be a difficult field, yet not barren of encouraging results to the patient worker.

To begin the theme of immunity, one must at once discard the meaning of absolute protection usually conveyed by it and employ the expression "relative immunity," or, better, "heightened resistance." We know, so far as tuberculosis is concerned, that in man no absolute immunity has been observed, meaning by this, *effective resistance throughout life*. The actuality is quite otherwise;

[1] Harvey Lecture, New York Academy of Medicine, January 16, 1915.
[2] Ibid., 1906, Jour. Amer. Med. Assoc., April 28, 1906.

yet many individuals unquestionably attain it in a practical sense in that no disease follows infection with tubercle bacilli.

From the pathologist's view-point few escape the formation of tubercles from the introduction of the bacilli. Even the nearly refractory animals, like the goat, cat, or dog, form primary foci. The immunity is thus not against infection but against its further spread. On the other hand, by the extensive observations of Harbitz,[3] Bartel,[4] and many others we know that living tubercle bacilli may lodge in the lymph glands for a considerable time without producing infection or tuberculous tissue. Doubtless many are disposed of before they have a chance to multiply. Nevertheless, given the proper conditions for multiplication and a bacillus of sufficient virulence or adaptability, it is perfectly conceivable that a single bacillus may suffice for infection. We must keep in mind the reciprocal relations between host and parasite, so well emphasized by Professor Smith, to understand why an infection may be balanced by the defenses and fail to make headway beyond the primary focus or port of entry.

Some of the conditions favorable to immunity are fairly defined; others elude our search or can only be stated in vague terms. Inoculated bacilli will at least act as irritant foreign bodies, unlike most bacteria, owing to their waxy substance; yet we can be certain that small numbers of bacilli, for example, or those of low virulence for the species, will hardly produce a focus at all, or if such is formed it will soon be encapsulated or absorbed.

On the part of the body, maturity of tissues, freedom from trauma (including such as is produced by inoculation), normal nutrition, and the absence of any exhausting malady or other toxic influence, constitute factors of safety of first importance.

On the other hand, right here we must remember that whatever balance or adjustment may take place *after* tubercle bacilli have established a lodging place in the tissues, no *specific* natural defenses existed so far as we know when they entered. The bacillus undoubtedly has an advantage here, because, given virgin soil and a race of bacilli already adapted to the species, an initial infection takes place with little hindrance from the non-specific defensive powers. The further history of such infections depends in part, at least, upon the amount of specific resistance aroused.

Natural Immunity. It has always been easier to define disposition to tuberculosis than immunity. Volumes have been written and an enormous literature has accumulated on the subject of disposition, yet something can conceivably be said for natural or acquired immunity in the qualified sense here used.

Certain species are relatively immune to strains of bacilli occasionally pathogenic for them. The horse and mule, for example,

[3] Jour. Infect. Dis., 1905, ii, 143. [4] Cent. f. Bakt. (orig.), xxxviii, 154.

are rarely infected by the bovine bacillus that occasionally may produce disease in them under constant exposure and sufficient dosage. Likewise, swine and sheep are ordinarily resistant to human infection. It does not seem difficult to explain these instances on the ground of non-adaptability of the parasite to races other than those forming its usual habitat.

The tubercle bacillus, especially the mammalian type, has, however, shown a rather widespread parasitic power as compared with other pathogenic organisms. It adapts itself also to many kinds of culture media in the laboratory, and there is practical agreement as to the existence of modifications of the two main divisions, human and bovine, Hence when any individuals of a race can be infected we can hardly speak of a natural immunity to all strains of tubercle bacilli.

Some ingenious explanations of the immunity of certain races and species have been propounded. As an example, a plausible theory for the immunity of a certain caterpillar of the bee moth is given by Metalnikoff[5] as the digestive power for wax with which the insect is endowed. Considerable experimental work is adduced by the author to support this idea of the mechanism of protection.

That cellular ferments of lytic character play a prominent part in natural resistance to bacterial infections is a convenient assumption. Otherwise there are temperature conditions, chemical and physiological differences, that can conceivably interfere with the growth of tubercle bacilli in highly resistant animals. We are obliged to leave the question unanswered by any formula capable of demonstration.

So far as man is concerned no race has been discovered that exhibits high natural resistance. The true explanation of any observed differences is quite different, as will be referred to later.

Some observations have been made tending to show a natural resistance in the Zulu natives of Natal, South Africa,[6] also of certain French families.[7] Such instances may be dismissed on the ground that opportunities for infection were limited.

Inherited and Acquired Immunity. A consideration of inherited and acquired immunity is more important in its practical results.

Some experimental work has been directed to the solution of the problem as to whether a susceptibility or immunity can be transmitted to offspring of tuberculous animals. No conclusion favorable to immunity to my knowledge has so far been made. The universal observation is that during an active stage of the disease a tuberculous mother has borne weak offspring, which if not, as a rule, tuberculous, often succumb to marasmus or are maldeveloped.

[5] Zeit. f. Immunität. (orig.), 1914, xxii, 235.
[6] Allen, J. F., Lancet, 1901, clxi, 198.
[7] Dubousquet-Labordoree, La Sem. Méd., 1897, xvii, 307.

If any form of specific resistance is conveyed from mother to young it is too much masked in these cases to be discovered.[8]

The toxic influences on the fetus from maternal disease are added to those affecting the germinal cells before fertilization. Consequently the anti-infectious or antitoxic principles if present are overshadowed.

In point of fact, as stated by Adami,[9] an actual specific immunity acquired by inheritance must be proved through the male parent. "It is essential to immunize the male parent alone, and that through a series of successive generations; and what is to be expected under these conditions is a Mendelian inheritance, certain of the progeny being immune, others not."

From the maternal side we know that substances derived directly from the bacilli can pass through the placenta in one form or another, together with antibodies produced in the mother. The results are disastrous to the young as in the experiments of Carrière,[10] and Maffuci,[11] who injected healthy guinea-pigs with extracts of tubercle bacilli. More than two-thirds of the offspring were either stillborn or died in two weeks. Schenk[12] claims to have demonstrated antibody by means of complement fixation in the offspring of normal and tuberculous guinea-pigs treated with bacillen emulsion. In my own experiments, in association with Dr. A. K. Krause,[13] the inheritance of anaphylactic sensitiveness was demonstrated by injecting pure tuberculoprotein into young guinea-pigs.

These experiments do not, of course, directly relate to the problem of most interest, and that is whether individuals who recover from tuberculosis can transmit any specific resistant quality, be it humoral or cellular. Several authors have assumed the presence of antibodies in the milk of vaccinated cows, which may fairly be considered as recovered animals while their immunity lasts. Von Behring, in 1903, suggested this, and because of the known secretion in the milk of antitoxins for other diseases (tetanus) considered the possibility of a transient passive immunity obtainable in this way. No experiments were published to my knowledge, nor has it been claimed that the calves born of the vaccinated cattle have shown unusual resistance to natural infection.

The only published work that I have found showing either an active or passive resistance in tuberculosis conveyed by milk is that of W. L. Moss,[14] and S. H. Gilliland.[15]

[8] The theory of inherited and acquired "lymphatism" expounded by Bartel comprehends an inherited resistance, though exhibited by a changed form of tuberculosis. Bartel, J., Probleme der Tuberkulosefrage, Deuticke, 1909.

[9] Principles of Pathology, 1910, 2d edition, i, 194.

[10] Arch. d. méd. exp., 1900, xii, 782. [11] Baumgarten's Jahresb., 1902, xxviii, 471.

[12] Folia Serol., 1909, ii, 343.

[13] Studies from Saranac Laboratory, Jour. Med. Res., 1910, xxii, 189.

[14] Transactions National Association for the Study and Prevention of Tuberculosis, 1914, x, 221.

[15] Ibid., p. 228

The former reported on a few calves fed on milk from vaccinated cows. There was a slightly favorable influence. Gilliland mentions a similar experiment with pigs fed on the milk of immunized cows in 1904–5, also suggestive of some protection. Neither experiment was very satisfactorily controlled.

So far no evidence of an experimental nature has shown any form of active immunity to be transmissible. It is quite true, too, that a truly specific disposition, acquired by inheritance, lacks an experimental basis. Here again the bovine race gives a negative to the assertion that tuberculous infection necessarily involves a transmitted weakness or susceptibility. On the contrary, breeding from tuberculin-reacting cows is actually practiced as of eugenic value in preserving the best stocks. The well-known Bang system has been on trial long enough in Denmark to have demonstrated its value, and is, I believe, the approved method of procedure in valuable dairies where tuberculosis is a serious menace.[16]

The observations on cattle here mentioned will not be conclusive that either resistance or susceptibility are stamped on the calves in one generation, but after the lapse of time the future generations should give an answer. They seem to me of great potential value at least in deciding whether the future generations will continue to be affected with the mild form of tuberculosis now prevalent and only discoverable by the tuberculin test.

Then, too, the non-inheritance of tuberculin sensitiveness as such leaves an opportunity for the discovery of some other hereditable quality, specifically adapted to favor or oppose the bacillus. (I shall again refer to the relation of tuberculin reactivity to immunity in connection with the clinical aspect of the problem.)

To make the assertion, finally, that there is no experimental basis for an inherited immunity or disposition does not mean that it is wholly impracticable to reach results of value, though admittedly difficult and wearisome to carry on such work successfully.

We must turn for the present to the biologist, the hygienist, or the statistician, as well as the historian, for further information. Immediately we find opposing views and many facts adduced to support each position. The matter is complex when inquiry is applied to families and races, and not less so in individuals.

Martius[17] took this view, and considers the statistical method inadequate to decide for or against a specific inherited predisposition or immunity. Hueppe[18] believes that both may be inherited, also certain organs show inherited predilection or the opposite for the tubercle bacillus. The latter, at least, has clinical observations to support it.

[16] A recent contribution by Harlow Brooks (Amer Jour. Med. Sci., 1914, cxlviii, 718) testifies that no defects were inherited from a tuberculous cow of unusual milk capacity.

[17] Berlin. klin. Woch., 1901, xxxviii, 814.

[18] Harben Lectures, London, 1903.

Turban[19] showed what he considered an inherited *locus minoris resistentiæ* in the large proportion of pulmonary cases where the morbid process began in the corresponding lung in parents and children. I was able to corroborate this observation in sixty-three families.[20]

I can only mention here some more recent noteworthy works on the subject of heredity in tuberculosis.

Cornet,[21] as is well known, has always scouted any belief in disposition.

Schlüter,[22] in a monograph of considerable size and value, concludes that there is no well-defined specific disposition.

Boeg[23] in studies on the Faroe Islanders gives no support to hereditary disposition.

Grunberg,[24] in a study of 568 families also found no specific heredity.

On the opposite side stands Karl Pearson,[25] the statistician, who by means of strictly mathematical rules applied to 384 families proves a clearly marked family inheritance of diathesis. It is impliedly a specific inheritance, though this appears an unnecessary assumption to me, considering that physical defects from other causes probably form an equally weak resistance and should be considered in estimating the specific element. Practically I think we must accept his conclusion that tuberculous families carry along more of the factors regarded as predispositions, and comprehended under the vague term "diathesis" than the average non-tuberculous family. Insurance interests must necessarily make their rules on the basis of such methods of study. But for the purpose of this lecture, I have only considered evidences of specific resistance, inherited or acquired, and therefore we can hardly confine the study to family groups and a few generations.

In passing, however, it may be of interest to note that such an eminent clinician as Herman Weber,[26] who believed in the heredity of tuberculosis, accepted insurance risks among the fibrous and so-called gouty tuberculous persons, thus recognizing their staying powers in the wrestle with the bacillus.

Leaving the question of family and individual inheritance for the moment, I will briefly mention the racial question. Reibmayr,[27] in an interesting monograph twenty years ago made a fair argument that a gradual process of immunization was taking place in the white race under civilized conditions. His reasoning was that owing to greater care, more weakly children survived to become tuberculous. The disease was consequently more widely spread,

[19] Zeitsch. f. Tub., i, 30, 123.
[20] Yale Medical Journal, 1902, p. 215.
[21] Die Tuberkulose, 2d Auf., 1907.
[22] Die Anlage zur. Tub., 1905.
[23] Zeitsch. f. Hyg., 1905, xlv, 161.
[24] Inaug. Thesis, Paris, 1912.
[25] Draper's Company Memoirs, 1907, ii; also Coring, Charles, ibid., 1909, v.
[26] Medical Examiner, 1898, p. 122.
[27] Die Ehe Tuberculosis u. Ihre Folgen, Wien, 1894.

but it developed chronicity as a sign of increasing resistance. Uncivilized races by contrast exhibited only acute forms of the disease of short duration. The infection is thus limited in extent. This theory admitted the paradox of a disposition and immunity (only relative, to be sure) in the same individual, and in my opinion has much to support it in clinical observation.

Many reports about tuberculosis in late years establish the fact that uncivilized races and those isolated for centuries from the chance of infection, develop acute forms of the disease when exposed. An excellent review of this subject was recently made by Maurice Fishberg,[28] whose well-known studies on the epidemiology of tuberculosis in the Jewish race have shown a decreasing mortality for many years in spite of their ample opportunities for infection. No doubt other factors—indeed, almost countless reasons other than a specifically acquired resistance—may tend to minimize the important conclusion that past generations of Jews have passed on an increasing resistance.

Enough evidence remains, I think, to accept the principle involved which Fishberg elucidates in his recent article, namely, that "the fatality of tuberculous infection depends on the length of time the ancestors of the affected people have been acquainted with the disease."

This principle is accepted with reference to other diseases, such as syphilis, malaria, and yellow fever, and is a rational inference from the known facts about tuberculosis.

There are, however, such marked exceptions to such a generalization that one must consider large groups rather than individuals. There are also other explanations of the relative mildness of epidemic diseases (as mentioned by Professor Theobald Smith) due to the disappearance or weeding-out process of the weaker individuals and races, both of host and bacillus.

I am more impressed, however, with the variability in resistance shown by man than by that of the bacillus. We may leave the subject of racial immunity, in my judgment, with a feeling of hopefulness that some progress has been made in the history of mankind, however slow, toward a self-protection. In this epoch, at least, the bacillus has not appeared to keep pace as an increasingly dangerous parasite.

Artificial Immunity. If the question of inherited predisposition or immunity is so difficult of answer, we yet have evidences of an artificially acquired immunity in the life of the individual. An endless amount of work has been done in laboratories and clinics to demonstrate this. A review of even the most important work would not be appropriate here;[29] it is enough to declare that

[28] New York Med. Jour., September 12 and 19, 1914.

[29] A most satisfactory review may be found in the Kolle-Wassermann Handbuch, 1913, 2d Auf., Bd. v.

up to now no satisfactory method of active or passive protection has been discovered which applies to man. Nevertheless, I should like to discuss some of the recent contributions to the subject, and especially the reasons for failure as well as partial success. Finally, the application of the knowledge is of value in interpreting clinical tuberculosis.

Since the disappointment with the vaccination of bovines and serotherapy for tuberculosis the conviction was borne in upon us that only transient protection could be attained, and this chiefly by a vaccine in which the vital spark was not quenched.

Since the time human bacilli were ruled out for use in vaccinating cattle, owing to the short duration of immunity, and their ability to get into the milk, other races of acid-fast bacilli have been put forward for protective inoculation. The feeble resistance obtained in this way merely confirmed previous experiments with them.[30]

McFadyean,[31] of Edinburgh, has more recently advocated avian bacilli for cattle vaccination because non-infectious for human kind, a doubtful assumption considering the occasional presence of such bacilli in tuberculous patients.

Webb[32] even ventured living human bacilli, trusting to small numbers gradually increased in children to avoid infection. This was found impracticable.

The results also with bacilli killed with very gentle heat[33] or devitalized by soap,[34] glycerin,[35] sugar, etc., have been but slightly encouraging thus far.

Vaccines made from the different elements of tubercle bacilli (von Ruck[36]) or from solutions of their substance (Deycke and Much[37]) have also failed to show any advantages over previous tuberculins used for immunization.

The significance of a living vaccine as compared with all substitutes has at present a close parallel in the now much-discussed *immunity from infection.*

The opinion is justified that mild infections are responsible for the considerable immunity hitherto observed in animals inoculated with weak-virulent living bacilli. These mild infections are closely comparable to those spontaneous ones from which the large proportion of our urban population recover. The results of bovine vaccination further justify the opinion that such protection as is con-

[30] Weber and Titze, Tub. Arb. a. d. Kais. Ges.-Amt., 1907, No. 7; Klimmer, M., Beit. z. Klin. d. Tub., 1910, Bd. xvii; Friedmann, F. F., Berlin. klin. Woch., 1912, xlix, 2214.

[31] Jour. Comp. Pathol. and Therap., 1913, xxvi, 327.

[32] Jour. Med. Research, 1911, xxiv, 1.

[33] Klimmer, M., Beit. z. Klin. d. Tub., 1910, Bd. xvii; Smith, Theobald, loc. cit.

[34] Noguchi, H., Jour. Exper. Med., 1910, p. 235; Zeuner, Cent. f. Bakt. (orig.), 1909, l.

[35] Levy, Blumenthal, and Marxer, Cent. f. Bakt. (orig.), 1906, p. 42; 1908, p. 48.

[36] New York Med. Record, August 31, 1912.

[37] Beit. z. Klin. d. Tub., 1910, xv, 277.

ferred depends on the presence of living bacilli or tuberculous tissue in the animal. This protection gradually wanes or disappears with the absorption of the bacilli or the tuberculous tissue.

The above statement being granted as based on experimental grounds, we may first observe that a spontaneous vaccination of human beings is in progress owing to wide-spread opportunities for infection. Many slight infections must be effective if we will interpret the healed tubercles in that light when found at autopsy. Unfortunately, neither the virulence nor the dose is controlled; hence progressive infections will occur in a considerable proportion of people. If both factors were under control and repetitions of mild infections obtainable at proper intervals it is imaginable that much good would result. Since we cannot assure a stability of virulence for inoculated bacilli, such a dream is far from realization. But we may again inquire, Why is the living bacillus necessary? Cannot the dead bacillus persist a long time in the body and produce tubercles (as we know to be true)? If tuberculous tissue is needed why not use dead bacilli?

The answer is difficult, but it is not likely that the dead bacilli persist long (except when shut off in the form of encapsulated nodules where large clumps may lodge). The tissue changes are also probably less pronounced and certainly more transient. I will also venture the theory that ferments in the living bacilli play a part. Until recently the presence of any function of ferment nature in the tubercle bacillus failed of demonstration. Through the studies of Wells and Corper[38] and those recently published of Kendall[39] and his associates, the presence of a lipase or fat-splitting ferment in the bacillus appears certain. Reciprocal and antagonistic ferment activity on the part of the bacillus and tissues is doubtless a better means of producing an immune reaction than when the ferment action is one-sided.

The studies of Opie[40] in this country, and later those of Manwaring,[41] support the belief that cell ferments combat the tubercle bacilli. Furthermore, the antibodies such as specific lysins are not readily demonstrable in the blood, yet their presence both in the leukocytes and fixed cells cannot be questioned. During a short period following inoculation the blood may contain some specific lysin, though it has not been fully recognized *in vitro*.

Roemer[42] was able to protect two sheep with the serum of another inoculated sheep; later this transferred immunity failed, probably because no serum lysin was left in the vaccinated sheep (some months after inoculation).

The "partial" serum antibody theories of Much[43] and others, while plausible in theory, seem to lack well-controlled experimental

[38] Jour. Infect. Dis., Chicago, 1912, xi, 388.
[39] Ibid., 1914, xv, 443–471.
[40] Jour. Exper. Med., 1908, x, 419.
[41] Ibid., 1912, xv, 1; 1913, xvii, 1.
[42] Deutsch. med. Woch., 1914, xl, 533.
[43] Ibid., xl, 554.

demonstration. In truth, no serum antibody[44] in tuberculosis has been definitely associated with immunity; in all experiments the cellular influences appear predominant.

A most interesting confirmation of this veiw was obtained by Manwaring and Bronfenbrenner,[45] who demonstrated lytic properties in the fixed peritoneal cells of animals. On the other hand, with the serum of vaccinated horses, Ruppel[46] obtained evidence of protective substance of antitoxic nature.

Hypersensitiveness or Allergy. There is another phenomenon intimately associated with immunity from tuberculous infection with which much speculation and many experiments have been made. This is the hypersensitiveness to tuberculin and especially to reinoculated tubercle bacilli, to which the term "allergy" was given by von Pirquet. It appears to be an important protective mechanism and probably a specific ferment action called forth from the leukocytes and fixed tissue cells by the presence of the invading bacillus or its derived substance.

The similarity and difference between the tuberculin reaction and the tissue reactions following inoculation are being much discussed at the present time; also the analogy to the anaphylactic reactions.

Reviewing the work on the artificial immunization of animals and the attempts to transfer anaphylaxis in tuberculosis, I think we can conclude that the mechanism is the same for all these phenomena. The differences in the manifestation of the reactions are chiefly explained by the presence of focal deposits of tubercle bacilli which can be regarded for comparison in the light of solid particles of foreign protein peculiarly difficult for digestion by the cellular ferments.

It is difficult to understand the cutaneous reactions, and most authors do not consider them anaphylactic manifestations. Unlike the majority of the latter, the skin sensitiveness as well as that of other tissues in a tuberculous animal is dependent upon the presence of tuberculous tissue or tubercle bacilli. Remove the bacilli or the tubercles and one finds that this form of sensitiveness disappears, and with it apparently all specific immunity to the disease is soon lost. The same thing happens when tubercles become thoroughly fibrous or calcified. In the changed reactivity, or the allergic inflammation, therefore, we have the essential features of the relative immunity of whatever grade, acquired in tuberculosis.

It is plain from these facts that a special form of sensitization is produced in tuberculosis by the cellular activities about the bacilli

[44] The "anticutines" of Loewenstein and Rappoport (Deutsch. med. Woch., 1904), and the hypothetical antitoxins of Sahli (Tuberculin Treatment, 1912) are too uncertain for demonstration, if indeed such exist.

[45] Jour. Exper. Med., 1913, xviii, 601.

[46] Zeits. f. Immunität. (orig.), vi, 344.

which radiates gradually to distant tissues not necessarily touched by the bacilli as such. Dead bacilli will act temporarily in this way, but pulverized preparations and extracts appear too fleeting in their effects to arouse it. They do nevertheless cause a true anaphylactic sensitiveness without skin manifestations, but unaccompanied by any recognizable immunity. The inflammatory reaction following inoculations of immune animals is the prominent feature, and is conspicuously absent in the others. Hence, we are justly entitled to the opinion that the cell accumulations about the bacilli are performing the duty of dissolving them or restricting their growth. The lymphocytes and endothelial cells have thus received much attention in connection with the tubercle bacillus inasmuch as they show lipolytic activity. The former are especially the reacting cells about the actively spreading foci of disease. Bartel[47] was one of the first to recognize the import of the lymphocyte reaction, and many facts have since tended to confirm it. (Opie,[48] Manwaring,[49] Kling,[50] Bergel,[51] Webb.[52])

No less important are the endothelial cells in connection with the fixation and absorption of the bacilli as histological studies show, by vital staining methods.

Some recent contributions are noteworthy. Lewis[53] found by the removal of spleen in white mice that a considerable increase of resistance was created to bovine bacilli. A rapid increase of lymphocytes following the removal of the spleen, due to hypertrophy of lymphoid tissue, is a possible explanation. On the other hand, Murphy and Ellis[54] of this city have exposed white mice to Roentgen radiation to destroy their lymphoid tissue and cells with the result that a tuberculous septicemia could be produced as compared with focal disease in control animals.

Much more may be said in relation to cell reactions and hypersensitiveness as a measure of resistance as well as the participation of humoral antibodies or ferments in the reactions.

These may be mentioned in connection with clinical observations.

Clinical Evidences of Immunity. We will now direct attention to a somewhat modern, possibly to some a novel, interpretation of tuberculosis in the symptomatology of the patient.

If our knowledge by experimental methods and observations is to be of value, we should expect to find signs of specific resistance under natural conditions of infection. This term "immunity" is seemingly too strong when used in describing such signs, but when we can discern that life is possibly conserved, and surely

[47] Cent. f. Bakt. (orig.), xl, 48.
[48] Jour. Exper. Med., 1914, xx.
[49] Loc. cit.
[50] Zeits. f. Immun., 1910, vii, 1.
[51] Zeits. f. Tub., 1914, Bd. xxii, 343.
[52] Transactions of the National Association for the Study and Prevention of Tuberculosis, 1910, Sixth Annual Report).
[53] Jour. Exp. Med., 1914, xix, 187.
[54] Ibid., xx, 397.

prolonged, by the defensive functions, it may not be amiss to employ that word.

Tuberculosis from the standpoint of the immunologist is possibly the best illustration of auto-immunity to an infectious agent. From this position we may divide tuberculous infections into four classes:

1. Those which recover without spreading or metastasis of the bacilli.
2. Those which continue to spread acutely, unresisted.
3. Those which progress in a slow chronic form.
4. Those which intermittently progress, becoming arrested in the intervals.

Each form may pass into another in all possible variations.

The types of each are recognized by symptoms except the first. This may only reveal itself by the various tuberculin tests or at postmortem.

It is most important from the point of view above taken, *i. e.*, from that of immunology, that the white race, at least, has for many centuries found a way to recover from repeated infections. We know that the chance of recovery increases from the second year of life to puberty in childhood infection,[55] depending on numerous factors, such as frequency of exposure, amount and virulence of the bacilli, intercurrent diseases, trauma, etc.

We also know that the majority of first infections involve the deeper lymphatic glands, not being resisted at the path of entrance. The course of events from this time forth is of exceeding interest from every standpoint.

We can then trace the path of infection thus far with fair certainty whatever the path of entry. But owing to the allergic state now induced, and which is known to be almost universal in ages over fifteen years (in greater or less degree with exposed families), we find it difficult to associate future disease with a new, exogenous infection. This is a problem about which discussion continues, and which is an important hygienic question.

Exposure to danger of massive infection without disease development in some instances can be ascribed to auto-immunity from earlier slight infections. In other instances it appears to be the cause of later pulmonary tuberculosis of the open ulcerated form occasioned by surface infection.

Both experimental and statistical studies have been brought to bear on this problem of reinfection, the first notably by Hamburger[56] and Roemer.[57] Pathological studies have seemed to give

[55] Hamburger, F., (Wien. med. Woch., 1914, No. 15) considers all infections in infants under one year develop into progressive disease and 50 per cent. of those in the second year. In ages over four years infection is rarely followed by progressive disease. Only 2 per cent. are found between eleven and fourteen years with an active form of tuberculosis.

[56] Beiträge z. Klin. d. Tub., 1910, xiii. [57] Ibid., xvii, 383.

rather uncertain results with reference to the question of new exogenous infections. Recently, however, a few cases have been found where the bovine type of bacillus has been isolated from one part of the body, usually a healed gland, and the human type from a fresh lung focus (Rabinowitsch).[58] Orth,[59] therefore, considers that such early bovine infections predispose to later human infections, yet the link is difficult to fit between them. Naturally, the question of changed type or virulence also comes into this problem.

Since old foci can break down and cause autogenous reinfection, there is reason to doubt the possibility of new exogenous infection in most cases. The acquired resistance to such a subsequent infection in adult life may be feeble after the complete healing of the old infections, which are usually confined to the lymph glands at the lung hilus or in the near vicinity. In those individuals, while the specific changes in reaction to tubercle bacilli seem to have been lost, when measured by a tuberculin test, we know the old allergy is latent, because in animal experiments reinoculations will arouse it even though no tuberculin reaction can be obtained. This is experimentally shown by intravenous inoculations, a rather extreme method, though we have a human parallel to it in the outbreak of an old focus suddenly rupturing into the blood stream, which is not uncommon in clinical experience. It is generally regarded inevitable that progressive miliary tuberculosis must follow this, and yet it is not necessarily true.

No doubt many of these cases occur, but the number of bacilli, their virulence and frequency in the blood stream, may confine the disease to the upper lobes of the lungs, where complete encapsulation may soon follow the acute febrile reaction. This is not usually regarded as a bacillemia, but we may readily consider it as such in the onset.

The commonly observed exacerbations or relapses in the course of tuberculosis follow the well-known "immune period" of two weeks in so many cases, that we may readily compare them to animals who overcome intravenous inoculations after a protective vaccination. In these it has been found that clumps of agglutinated bacilli are likely to lodge in some other organs, normally resistant to the germ (see Roemer[60]). The parallel may be carried yet further, for in the case of man some bacilli are apt to survive and form new sources of danger in other organs, later emerging as open ulcerations or latent in a soil of less resistance, that is, the lung.

Experience with cattle, sheep, and goats has demonstrated this in various ways, yet in cattle, adult pulmonary tuberculosis is regarded as a new infection from without, obtained in adult life for the most part.[61]

[58] Deutsch. med. Woch., 1913, xxxix, 105.
[59] Berlin. klin. Woch., 1913, l, 429.
[60] Beit. z. Klin. d. Tub., 1910, xvii, 287.
[61] Smith, Theobald, Harvey Lecture, 1906.

The grafting of new exogenous bacilli in the human lung in adult life nevertheless requires especially lowered health or enormous doses of bacilli. Specific resistance may run down to zero and yet the adult tissues seem naturally prepared for ordinary exposure to infection. Therefore, it is difficult to ascribe the immunity to any allergic state. This seems especially true after the lapse of tuberculin allergy due to complete healing of former foci.

Some inquiries have been made to determine the frequency of adult infection from new sources. In Breslau an investigation of sources of infection by Bruck and Steinberg[62] led to the opinion that both autogenous and exogenous infections caused the adult disease. Hillenberg[63] in a thousand tuberculous cases in the city of Leitz agreed with the above-named authors. He thinks it safe to say that those patients who develop the disease after the age of forty-five years, are due to later infection than childhood unless the disease was in the family. The relative infrequency of the disease in married partners he suggests as being due to a continuous process of immunization due to increasing exposure. The proportion of new infections among sanatorium and hospital staffs is so small that we may use the same explanation to account for it.

The facts anyway appear to show that frequent contact with the bacillus can occur without harm in adult life, and this is a comforting thought. This idea may be new to many who have become phthisiophobic, but a little reflection must arouse curiosity as to the vital resisting powers of many persons in constant contact with tuberculous patients!

As already noted, the absence of resistance in non-infected races ("virgin soil") is of some significance. Nor is it confined to uncivilized peoples, as many instances of acute tuberculosis are seen among healthy adults, particularly from rural districts.

I am not aware that the virulence of the bacillus in these cases is unusual, except for the individual involved. This is shown by the many instances of family infection of all grades of severity. In these the age and amount of infection at the time of primary infection are of great importance.

Whatever the immediate exciting cause of metastatic or fresh reinfection, the result is a higher degree of allergy unless miliary or acute pneumonic disease supervenes. We may note the symptoms of such resistance by the fever, stronger cutaneous reaction and hyperemia about the foci, as, *e. g.*, in the larynx. That the disease now continues to progress is not necessarily because of failure of the immunizing mechanism to act. There may be mechanical reasons, such as trauma and overexercise that cause the bacilli to spread, bringing new foci to the lungs, or elsewhere into the system of tuberculous tissue, thereby heightening the

[62] Zeitsch. f. Hyg., 1912, lxxi, 177.

[63] Zeitsch. f. Hyg., 1914, lxxvii, 101.

allergy until it reaches a maximum point. From this time a paradoxical state may prevail. The hypersensitiveness now causes a chronic poisoning by its constant activity, or rapid exhaustion occurs from the toxemia. On the other hand, we have reason to believe that but for this protective function miliary tuberculosis might occur oftener in a fatal form.

In recent years we have learned the fact that tubercle bacilli wash into the blood stream more frequently than was formerly considered possible, unless an acute miliary disease was present. It is highly probable that many such bacilli are weakened and dissolved by lysis without producing lesions—only causing anaphylactic fever. They may even aid in immunization if intermittently received, so that the dose at any given time can be overcome readily. For example, it is alleged that a tuberculin reaction can produce a bacillemia, which seems to me quite probable to a small extent, yet such a violent reaction as would lead assuredly to loosening bacilli from their moorings has been known to promote a rapid healing. It is not unknown to have other causes lead to strong reactions followed by improvement in the course of a progressive tuberculosis. Such stimulations to the immune reactions are obviously dangerous and unsafe when repeated often, and no experience is so disastrous as an "auto-inoculation" pushed too far, whether by natural means or by tuberculin treatment, artificially applied. It is significant, however, that physical and nervous exhaustion are the most dangerous sources of auto-inoculation.

Moreover, we are familiar with the healing of sluggish ulcers as the result of irritants directly applied, and even intercurrent disease causing the absorption and disappearance of tuberculous foci in the skin, glands, and occasionally elsewhere. The method of Bier by producing alternate passive and active hyperemia has much value and a correct rationale in the light of immunology as applied to tuberculosis.

Stimulation of foci in the lungs, however, requires clinical experience and judgment, for a highly vascular moving organ with, as we have seen, a possible selective affinity for cultivating the tubercle bacillus is to be treated cautiously.

There is often a delicate adjustment or balance in tuberculous disease after it has become arrested. Regarded as a problem in maintaining immunity, the tuberculous individual must be taught to patiently await the time when cicatrization can change the highly sensitive foci to fibrous tissue, before danger of relapse is lessened for those who retain the two-edged sword of hypersensitiveness in an active form.

Here we may refer to the strong contrast between a recently active tuberculosis and one of chronic, fibroid type. In the first there is need of strong lytic action to prevent dissemination of the bacilli. In the fibrous form the bacilli may be abundant in the

sputum, but so shut off from the blood that little allergy is present. These latter patients are true "carriers" of tuberculosis, but have no longer any symptoms of absorption from the focus, and consequently low capacity for reaction. They recover very slowly, if at all, but bear stimulation of all kinds more safely. I mention these contrasts for their suggestiveness in treatment.

Interesting examples of the healing of a tuberculous focus in one part of the body while an acute outbreak is in progress elsewhere can be mentioned as auto-immunity phenomena. This is occasionally observed in the larynx during a pulmonary exacerbation, and *vice versa*. The influence of pleural effusion in arresting intrapulmonary disease of the opposite lung is another illustration. The laryngeal swellings often diminish without reactive indications. Likewise, pulmonary ulceration may heal in the course of pleurisy, apparently with no increased inflammation. Immune bodies circulating in the blood best account for these cases, but I cannot offer a satisfactory explanation.[64] The use of autoserotherapy from pleural effusions has been considered rational, on the presumption that immune substances are present, but with what experimental proof I am uninformed.

Many other manifestations of auto-immunity could be cited, including all forms of surface ulceration in advanced tuberculosis, also the various cutaneous affections. These can only be grouped as consequences of the life-protecting functions but not happy in effects.

It remains to emphasize some of the points from which I may draw conclusions.

1. There is no natural immunity to tuberculosis in warm-blooded animals to the types of bacilli found in the bovine or human race.

2. There is a considerable variation in resistance in some species probably due to the chemical effect of their secretions or physiological differences in the animals, but chiefly to the fact that the bacillus has not become adapted to long-continued parasitic existence in them.

3. In the human species no natural immunity is found in any race. All uncivilized races long removed from infection are very susceptible, but the white races, especially the European Jews, have acquired a certain degree of immunity by inheritance and almost universal infection. The rapid increase of intercourse between all lands and races facilitates the universal spread of tuberculosis, which is certain to occur through the medium of numerous bacillus "carriers."

[64] A few cases of completely arrested advanced tuberculosis following artificial pneumothorax with marked purulent pleurisy have suggested anew to me the importance of the cellular reactions in tuberculosis. The pus which contained tubercle bacilli alone, was repeatedly withdrawn and striking improvement in the intrapulmonary disease accompanied the effusion after it became full of leukocytes.

4. The ultimate survival of those who acquire a relative immunity will tend to diminish the severity of the disease, but many generations may be required to accomplish this.

5. The opportunities for infection, now universal in cities, will diminish gradually in civilized lands by lessening the danger from advanced cases, also from bovine sources. For many years, however, the number of "carriers" will increase owing to improved care, longer life, and higher standards of living among the people.

6. The best degree of resistance against tuberculosis that has been attained by experiments on the lower animals involves inoculation of living bacilli. This is of little value because of short duration of the protection and the danger of sequestered bacilli.

7. The natural infection of human beings takes place largely in childhood and increases the resistance to subsequent disease in a large measure. Under improved care of the tuberculous and better hygiene the amount and frequency of severe infections should diminish, while the number of those with slight, relatively harmless infections should relatively increase.

8. Adults withstand exogenous reinfection under extreme exposure, partly on account of slight infections in earlier life and favorable occupations, environment, and nutrition.

9. The specific immunity acquired from natural infection is largely due to cellular reactions of bacteriolytic nature, which take place outside the blood stream for the most part.

10. The interaction between the ferments of the body cells and those of the bacillus, lead to heightened activity of the lytic power, both lipolysis and proteolysis.

11. The tuberculin sensitiveness or "allergy" is the chief indication of specific resistance. In the patient most of the inflammatory symptoms are due to the actively working immunity functions.

12. In the therapy of tuberculosis this principle should be applied:

To avoid interference with Nature's powers of resistance when she is attempting to localize the infection with apparent success.

FEVER IN TUBERCULOSIS.[1]

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The contributions of physiology relating to heat production and heat dissipation, and the factors responsible for the mainten-

[1] Read before the Saranac Lake Medical Society, Saranac Lake, New York, Dec. 30, 1913.

ance of body temperature, are of special value for the correct interpretation of the pathology of fever. The special role of bacteria in the production of fever and the more recent work by Vaughn showing the part played by the toxic radicle of the protein molecule in the etiology of fever are also pertinent to the elucidation of this subject, and of paramount importance to the further development of a more comprehensive understanding of the basic factors in relation to fever. However, in the present paper, it is desired to emphasize only the clinical aspect of fever as observed in pulmonary tuberculosis.

Since temperature and fever are so closely related, it might be of interest to precede the discussion by a brief historical sketch of the thermometer. From earliest times the body temperature has occupied a place in the scale of heat measurements, and physicians have long recognized an increase in the blood temperature as a cardinal symptom of fever, although the degree of fever was measured by the pulse acceleration.

About 1610 Galileo constructed the first thermometer. This consisted of a glass bulb containing air, connected to a glass tube of small bore, dipping into a colored fluid. Owing to changes resulting from atmospheric pressure, this style of thermometer proved unsatisfactory. Some years later Galileo introduced a second type of thermometer, familiar to us at the present day, containing a liquid hermetically sealed in a glass bulb with a fine tube attached. In 1710 Isaac Newton proposed a scale, divided into twelve parts, in which zero represented the freezing-point of water and twelve the body temperature. Gabriel Daniel Fahrenheit, in 1714, in devising the scale now in general use, also employed the temperature of the human body as one of the major divisions of his scale. Traub, Baronsprung, and Wunderlich established the value of the clinical thermometer to medicine. From this period, about 1850, the clinical thermometer has become an important part of the physician's accoutrement.

Methods of Taking Temperature. The first requisite in taking temperature is a standard thermometer. Out of a series of eighty-three certified thermometers tested in a water-bath, seventeen showed a variation of from 0.3° to 0.6°. Comparative rectal readings approximated closely the discrepancies obtained by the water-bath. To corroborate these tests, six thermometers showing marked error were forwarded to the Bureau of Standards at Washington, D. C. The letter here reproduced needs no comment: "The Bureau begs to state that the five clinical thermometers which exceeded the limits of allowable error were in error by from 0.4° to 0.6° at different points. The readings of the thermometer which retreated were not recorded. As these instruments were so badly in error the sign of the correction was not carefully noted."

A further series of fifty-five were examined by the Bureau; thirty-five passed and twenty were rejected. To obtain an accurate reading irrespective of type of thermometer, demands a period of from five to ten minutes. Many authorities, including Walther, Nordrach, Penbold, and King, advocate rectal temperatures on account of greater accuracy. However, parallel determinations by Schroeder, Bruhl, and others have shown that the discrepancies between oral and rectal readings are so slight that they can be ignored. Conditions regulate the choice at times. Thus the rectum or axilla is preferable in children, the weak or acutely ill, patients suffering from marked dyspnea, oral or throat inflammations, and nasal obstruction. When fever is suspected, but not revealed by oral reading, rectal reading is indicated as control.

The disadvantages of rectal readings are obvious. The manipulations are distasteful, and in ambulant cases, necessitates the patient retiring to his room. Care must be taken that the rectum

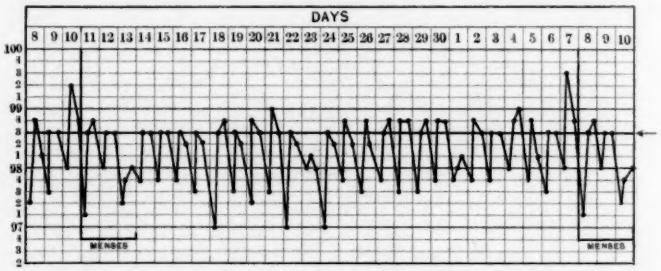

FIG. 1.—Case 2977. Female, aged nineteenyears. Premenstrual fever in an afebrile case of incipient tuberculosis.

is free from fecal matter. It has been shown that exercise has a decided influence on the rectal temperature, due presumably to the close approximation of the large muscles in this region. A preliminary rest is therefore especially indicated before rectal readings, as this method does not record the actual body temperature after exercise. The axilla still remains in high favor, especially in certain European centres. Cornet favors rectal temperatures and prefers axilla to mouth readings. Franck concludes that the axilla method of taking clinical temperature observations no longer meets the requirements of diagnosis on account of possible inaccuracies and the time required. He regards rectal measurements as the quickest and most accurate means. So good an authority as Turban is satisfied with oral temperatures, and he voices the consensus of opinion, at least in this country.

WHAT IS NORMAL TEMPERATURE? Since in no other disease are minor fluctuations of temperature of greater import, the establishment of the normal temperature range is the first essential in

determining the significance of fever in tuberculosis. A detailed study of the literature shows obvious disparities among authors in their ideas regarding normal temperature. The following tabulation by different authors gives the maximum normal:

Wunderlich: Axilla, 98.94° F.; mouth, 99.3° F.

Vierordt: Mouth, 99.6° F .

Turban: Mouth, 98.9° F.

Stewart: Axilla, 99.5° F.; mouth 99.1° F.

Foster: Axilla, 36° to 37.5° C.; mouth, 0.25° to 1.5° C. higher than axilla.

Finlayson: Mouth, 98.6° F.

Sahli: Mouth, 99.32° F.

Meyer states that oral readings exceeding 37.3° C. represent fever.

Schneider and Weise concur with this view.

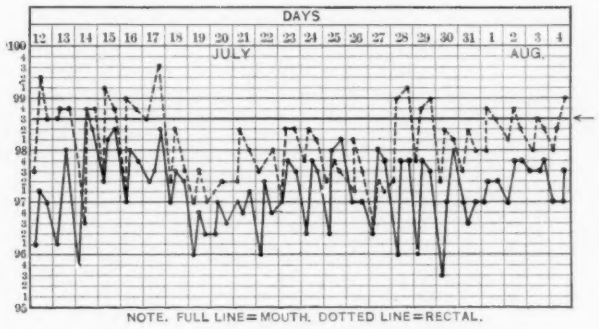

FIG. 2.—Case 3042. Female, aged thirty-seven years; stage three; progressive type. Comparative oral and rectal readings showing subnormal temperature.

Turban considers 99.3° F., if frequently recurring, as fever. Sahli says 99.32° F. is within physiological limits. This, in consumption, would correspond to a rectal temperature of 100.4° F., and so indicate fever.

The above discrepancies can hardly be accounted for by errors in technique. Sex, time of day, and season are not mentioned, and the possible inclusion by the older authorities of cases of early tuberculosis might offer a partial explanation. Notwithstanding these facts it is reasonable to suppose that normal temperature has a considerable range, and is of some moment in estimating the degree of temperature in tuberculosis.

The diurnal range is approximately 1.8° F. Any definite increase beyond this limit is considered by some as indicating fever. Thus we may have the paradoxical condition of a patient with fever and apparently normal temperature. The normal diurnal curve is

modified by exercise, food, seasonal change, the ingestion of hot or cold liquids, and psychical conditions, such as, anger, grief, and mental concentration. A physician of my acquaintance could, by matching himself against a worthy chess opponent, regularly raise his temperature over 100° F. Care must be taken to avoid misinterpretation of the slight premenstrual increase in temperature normally present in some cases. When slight fluctuations are present it has been suggested to take readings over a lengthy period, and by this means the normal range for any certain individual can be approximately obtained.

THE BACTERIOLOGY OF FEVER. In the bacteriology of fever in tuberculosis we are confronted by a complex problem which has not yet been completely solved. The toxins of the tubercle bacillus

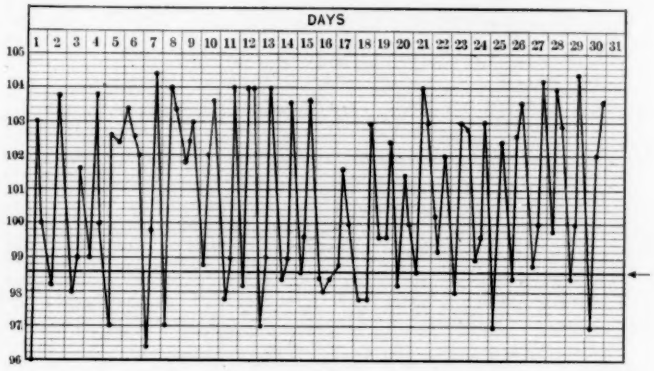

FIG. 3.—Case 2189. Female, aged twenty-six years; stage three. That the above hectic type of fever exhibiting such wide temperature variations is compatible with life for a period of months is clinically of decided interest, indicating that the prostrating action of the fever is more kindly borne in tuberculosis than in most other infections.

are capable in themselves of inducing fever. This is well exemplified in the tuberculin reaction, where the question of mixed infection is certainly excluded, and in the fever accompanying an exacerbation of a tuberculous process. For many years the exact role played by secondary organisms in the production of fever in tuberculosis has caused lively discussion; among such organisms may be mentioned the various streptococci, Staphylococcus pyogenes aureus, Friedländer's bacillus, influenza bacillus, and pneumococcus. They may be readily demonstrated in tuberculous sputum, and can be recovered at autopsy directly from the involved tissue. The question is one of indecision in individual cases, but we may, on clinical grounds, with some degree of certainty, assume that in certain cases, especially those in the terminal

stages, and exhibiting a hectic type of fever, are suffering from a mixed infection.

Character of Fever in Tuberculosis. Patients exhibit marked differences in their reaction to fever and to the clinician; the striking contrast between the apparent comfort of the patient and the temperature record forms one of the most marked peculiarities of the fever in tuberculosis. On the other hand, some patients, especially those with a neurotic tendency, are notably affected. The apparent selective action of the toxin is evident in some cases and may lead to error in diagnosis. The pulmonary lesion may remain latent, or apparently so, and yet evidence of intoxication appears in many cases. Thus we may see cases where the gastro-intestinal symptoms dominate the clinical field, obscuring

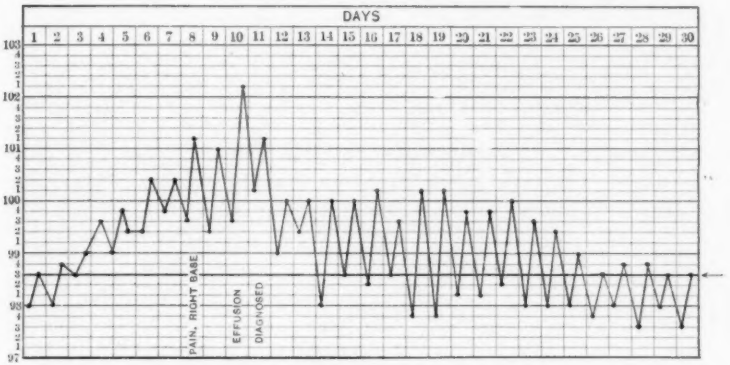

Fig. 4.—Case 2281. Male, aged seventeen years. After a gradual rise in temperature for a few days, onset of base pain; two days later effusion detected. The temperature reactions in cases complicated by pleural effusion are variable, but the above chart expresses, in a fairly typical manner, the reaction in those cases terminating favorably.

the real nature of the infection. At other times the condition may be masked by an accompanying neurasthenia. Disturbances of the circulatory system may lead to false conclusions, especially when anemia is present. A profound weakness may be the sole complaint for which the patient is unable to give an explanation. Finally, fever may be present in some cases with such slight constitutional symptoms that it escapes even the patient's notice.

Unfortunately no typical temperature curve exists in tuberculosis as in some other infectious diseases. The fever occurring at the onset can so closely simulate the typical temperature curve observed in certain other diseases, notably pneumonia, typhoid, and malaria, that error not infrequently arises, the further course of the disease alone suggesting the true nature of the causal agent. A certain type of initial fever, however, is worthy of mention, because

of its frequent association with beginning tubercle formation. It is distinguished by a slight post meridian temperature ranging from 99.2° F. to 100.2° F., evanescent, showing marked fluctuation and requiring two-hour readings for proper interpretation.

In a study of the temperature curve of pulmonary tuberculosis over a period of months the alternating febrile and afebrile states and the extreme irregularity of these intermittent periods, form one of the most striking characteristics. The curve also represents in some cases, fairly typically, the actual clinical course. In the progressive type the afebrile periods become shorter, the febrile correspondingly longer, with increase in the temperature range, and toward the end the fever generally assumes the hectic form, A reversal of the above picture in cases with a favorable outlook commonly occurs.

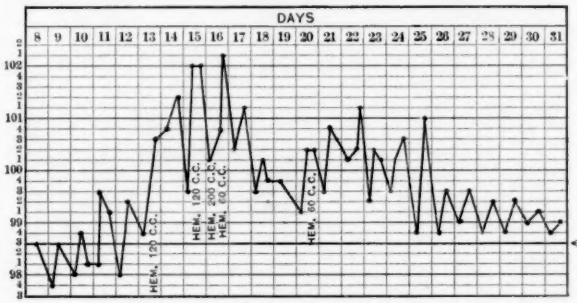

FIG. 5.—Case 2731. Male, aged twenty-one years. Hemoptysis with temperature. The frequent rise in temperature preceding hemoptysis is noted. Following the hemoptysis a considerable rise occured. On account of bacteriological difficulties the role of secondary organisms in the production of hemorrhages and their relation to the different types of fever has in our hands received no definite confirmation.

Williams, Minor, and others have drawn attention to the frequently accompanying subnormal temperature to which they attribute much importance. The temperature is extremely labile, oscillating readily to slight stimuli. Exercise can induce a decided rise in temperature, the reaction being more pronounced when little or no exercise has been previously allowed. Eating and mental excitement often lead to an increase in temperature.

The fever is arbitrarily divided into three parts, the divisions depending on the degree of temperature: First, from 99.2° F. to 100.2° F.; second, from 100.2° F. to 102.2° F.; third above 102.2° F. The fever may be continuous or remittent, but intermittent fever is the rule in tuberculosis.

The following tabulation of the temperatures of 223 cases admitted to the Ray Brook Sanatorium consists of two hourly readings from 7 A.M. to 9 P.M. for a period of eight days subsequent

to admission. To separate the febrile from the non-febrile cases it was necessary to establish some arbitrary rule in the following tabulation: all cases that presented a temperature of 99.2° F. or above on three separate days were classified with the febrile group:

Incipient, 107; febrile, 45 or 42 per cent.; non-febrile, 62 or 58 per cent.

Moderately advanced, 76; febrile, 44 or 58 per cent.; non-febrile, 32 or 42 per cent.

Advanced, 40; febrile, 32 or 80 per cent.; non-febrile, 8 or 20 per cent.

Average maximum temperature of 45 incipient cases, 99.8° F.

Average maximum temperature of 44 moderately advanced cases, 100° F.

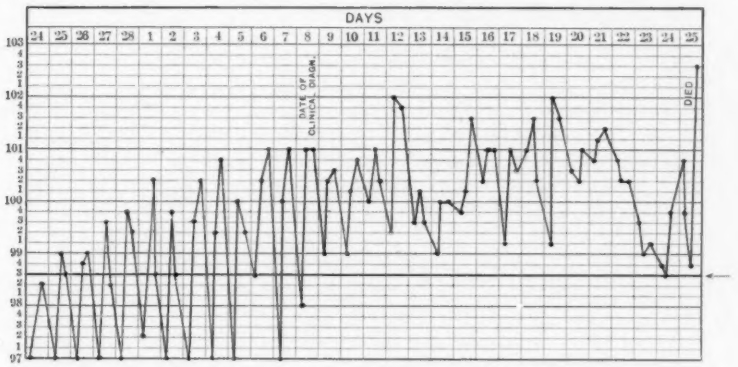

FIG. 6.—Case 1665. Male, aged twenty-one years. Pulmonary tuberculosis; stage two. Symptoms quiescent, excellent nutrition. Diagnosis of meningitis two weeks after onset of fever. The effect produced on the temperature curve by the meningeal complication is well illustrated.

Average maximum temperature of 32 advanced cases, 100.4° F.

The selection of patients for sanatorium treatment probably exercises a decided influence on the above figures, since the acutely ill are excluded. Nevertheless, these figures indicate that the percentage of febrile cases and the degree of temperature increase with the stage of the disease.

An endeavor has been made to establish a connection between fever and the stage of the disease, and, *a priori*, there would seem justification for this classification, since the degree of temperature should be closely related to the amount of lung infiltration. However a considerable number of cases cannot be so classified. The degree of saturation of the blood and tissues with toxin is in direct proportion to the absorptive powers of the contiguous tissues

surrounding the focus. Their ability or inability to impede peripheral absorption is one of the factors which determine the degree of fever present. Concerning a second factor the protective substances generated by the tissues, nothing definite can be said, but clinical experience would lead us to believe that fever is also definitely influenced by these agents. Furthermore, individual susceptibility of the heat-regulating centre must be remembered. These factors, peripheral absorption, the presence of protective substances, and the condition of the heat regulating centres offer some explanation why certain cases with a slight initial lesion show grave constitutional symptoms, while others with gross pulmonary lesions may remain afebrile.

Miliary tuberculosis requires special consideration, in that a considerable degree of temperature is usually present at the onset and may be ushered in by chills, with rapid rise in temperature to 104° F. or above. The pyrexia may persist in the form of a continued fever, can assume an irregular remittent character, or, for short periods, be intermittent. The entire course of the disease may be characterized by moderate or even slight elevations of temperature. The typus inversus morning temperature with afternoon decline, according to Brunnechi, is characteristic of this type of tubercle invasion.

Factors which Influence the Temperature. Sudden relatively high temperatures of short duration are commonly the result of non-tuberculous complications, throat inflammations, gastro-intestinal disturbances, etc. Tuberculous meningitis often has a depressant influence on the temperature and may give rise to decided fluctuations. Profuse hemorrhages and continued diarrhea often cause a fall in temperature. The temperature invariably registers higher after an exacerbation of the local inflammatory process, pleurisy, aspiration, following hemorrhages, etc. The anatomical position of the lesion has apparently no direct bearing on the temperature. The favorable effects resulting from cardiac insufficiency has been pointed out by many observers, and is explained on the basis of pulmonary stasis.

Diagnosis. The determination of fever is of great clinical value, forming, as it does, the cardinal index of the constitutional symptoms in tuberculosis, and one of the earliest and most reliable indications of tuberculous implantation. Since slight fluctuations of temperature are of great diagnostic value the question arises, at what point on the thermometer does normal temperature end and fever begin? Owing to the variability in the normal temperature as above mentioned, only an approximate estimate can be made in a given case; roughly, the maximum normal temperature ranges between 98.6° F. and 99.4° F.

Experience would seem to indicate that a mere transitory rise of temperature can be ignored in diagnosis, as various obscure

factors may play a part in its cause. Slight elevations of temperature, 99.2° F. to 99.4° F., however, if persistent or recurring frequently, become of diagnostic value.

The extreme variability of the temperature curve in pulmonary tuberculosis materially decreases its value in diagnosis. Cornet says, "A temperature of 99.8° F., which is intermittent but obstinate, and which increases upon the slightest exertion, indicates tuberculosis unless some other etiological factor can be discovered." This is a satisfactory rule, but must be applied with caution, since not infrequently the other etiological factors can be excluded only with difficulty. The forwarding of patients to sanatoria because of an unexplained temperature, which later proves itself to be non-tuberculous, is not infrequent.

There are a few diseases in which the temperature curve so closely simulates that of pulmonary tuberculosis that a differential diagnosis is of extreme importance. These diseases may be classified as pulmonary and extra-pulmonary. In the first group the disease most frequently leading to error is influenza. The bacteriological examination is often the only available means for differentiation. Other conditions of less frequency are lung abscess, syphilis, actinomycosis, bronchiectasis, occasionally mediastinal tumor, and malignant disease. In the extra-pulmonary group may be included Graves' disease, gastro-intestinal conditions, syphilis, certain cardiac conditions, Hodgkins' disease, cryptic suppurations, malaria, and typhoid. The differential diagnosis of Graves' disease is of special importance, and not infrequently cases are admitted to sanatoria with this mistake in diagnosis. Gastric dilatation, intestinal toxemia, and chronic appendicitis are confusing, in that functional changes of the digestive tract are frequent in pulmonary tuberculosis. The anemia, the loss of weight, the malaise, and even the fever of secondary syphilis, in the absence of rash, sore throat, etc., may strongly suggest the presence of tuberculosis. An irregular intermittent fever extending over a period of months in a certain group of cardiac cases has of late received attention, since the diagnosis of these cases has frequently been confused with that of tuberculosis. The fever that occasionally precedes the glandular enlargement of Hodgkins' disease, and which is so frequently accompanied by weakness, anemia, loss of weight, and anorexia extending over many weeks, has led to the erroneous diagnosis of concealed tuberculosis in more than one case. Local pus pockets, especially in the nasal sinuses, with latent local symptoms, are often confusing. In malarial districts the malarial type of fever in tuberculosis renders differential diagnosis difficult. The fever of miliary tuberculosis is similar in many respects to that of typhoid, and the differential diagnosis forms one of the most difficult problems in clinical medicine.

PROGNOSIS. In the prognosis of pulmonary tuberculosis, fever is a most reliable index of the ultimate course of the disease. Fever that resists treatment always speaks for an unfavorable outcome. The height and duration of the fever affect the prognosis correspondingly. The absence of fever does not, as is often accepted, necessarily imply improvement. Progression of the disease in the absence of fever can be clinically demonstrated.

CONCLUSIONS. 1. There is a necessity for testing the accuracy of certified thermometers.

2. Normal temperature may vary within considerable limits.

3. The selective action of tuberculo toxin in pulmonary cases may directly affect other systems than the respiratory, and thus lead to error in diagnosis.

4. The temperature curve in pulmonary tuberculosis is protean in character, and may simulate that of many other diseases.

5. Fever is the cardinal symptom of incipient tuberculosis: its nature and persistence are of diagnostic import.

6. The persistence of fever bears a definite relation to prognosis.

The appended temperature charts are presented to illustrate types of fever in tuberculosis.

EXUDATES IN ARTIFICIAL PNEUMOTHORAX.

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WHEN one has had the experience of seeing a Lazarus rise from the dead, the incident will never be forgotten, and the procedure which enables this to be done will not be abandoned even though such dramatic successes are but few in comparison with the whole number of cases in which artificial pneumothorax is performed. This method is still in the experimental stage, and many more years' experience will be required to more truly indicate its limitations as well as the type of case in which it is likely to prove most successful. The mechanical conditions met with in advanced tuberculosis, as, for instance, adhesions, consistency of the lung to be compressed, thickness of cavity walls, metabolic reactions to compression, the state of the other lung, the effect upon complications, particularly those of tuberculous character, the alteration of circulation, position of the heart, and the effect of pressure upon

the digestive organs, compose a picture of great complexity with an endless variety of factors introduced into the problem presented by each and every case.

One thing seems certain, compression has come to stay, and the problem facing phthisiotherapists is the delimitation of the method —to use it for the greatest good of the greatest number of consumptives applying to us for help. The purpose of this paper is to assist in a measure toward the elucidation of the problem of the application of artificial pneumothorax.

We thought at first that our cases were too few to enable us to draw any conclusions from our own experience in clarifying the problems of this treatment, but we find upon studying the literature that the number of cases in which we have employed this method during the past three years will compare favorably with those of other clinicians. To date we have had fifty cases. In 50 per cent. it was impossible to obtain an efficient pneumothorax on account of the mechanical conditions encountered, such as adhesions, etc. In a small number, even though a certain degree of compression could be induced, it was not effective as regards compression of the essential lesion—the cavity, etc. There has been about the proportion of really successful cases that other observers have noted. From our experience we do not hesitate to draw two conclusions; one of them is that in certain of these cases in which a clinically effective degree of compression is impossible the procedure must be supplemented by surgery, and we think that the time will come shortly when a qualified surgeon will be necessary as an adjunct to the staff of every large institution for tuberculosis. The other conclusion is this: admitting, as we all do, that in something like 50 per cent. of the cases we cannot obtain an artificial pneumothorax on account of the mechanical conditions presenting, it seems to us very plain, indeed, that our efforts should be directed toward the anticipation of these extensive adhesions; in other words, that when a case presents the unqualified evidence of progression, especially in the presence of a relatively sound or arrested process in the good lung, that we should not wait until pneumothorax is forced upon us, but should perform this operation when it is not only mechanically possible, but when the organism is still capable of withstanding the effects of compression.

During the past year we have been trying to do this, and from the results already achieved we have little doubt that in a few years we will be able to prove, if it has not already been done, that the most successful pneumothorax cases will be those in which this method was applied in the comparatively early stages of advanced disease or in a progressive lesion not far advanced, when the conditions are of our own choosing and not relatively or wholly beyond our reach. It is all very well and gratifying to save an occasional far-advanced case by this method, but infinitely more useful to

prevent them in a larger proportion of cases from ever becoming far advanced, for under such conditions, as we all know, the method is grossly handicapped, not only by the 50 per cent. of instances in which it is no longer possible on account of the adhesions, but by the failure of the good or relatively good lung to withstand the effect of the pneumothorax, as well as by the unfavorable conditions presented by the body in far-advanced tuberculous disease, and also the possibility that complications, such as laryngeal or intestinal tuberculosis, the existence of which may have been previously unsuspected, may immediately become flamboyant in their manifestations upon the induction of a pneumothorax, though, as we all know, such complications, are as likely to be benefited as aroused to activity.

During the past year or two, as experience with this method has matured, we have heard more and more of the occurrence of exudates following pneumothorax; in fact, it is claimed by a consensus of opinion in Europe and America that in at least one-half of the cases in which pneumothorax is mechanically possible that ultimately an effusion will occur. It is but natural to suppose that the more extensive the involvement the more the pleura has been invaded by a tuberculous process; in other words the longer we wait the more likely we are to witness this phenomenon of effusion. An examination of the cases abroad definitely proves that this statement is true, and further substantiates our opinion that pneumothorax has other applications than are found in so-called hopeless cases. When we first read of the occurrence of these frequent effusions it was astonishing to us, for in but one of our 26 cases in which gas could be introduced effectively have we had a large effusion, and in but 4 an insignificent quantity of fluid, which in 1 was subsequently resorbed, and in 3 a small quantity still persists. Our physical examinations were controlled by fluoroscopic inspection. We asked ourselves, Is our experience unique? and if so, to what is it due? We communicated with the medical authorities at the United States Army General Hospital at Fort Bayard, New Mexico, and it proves that their experience has been as follows: of 19 cases in which artificial pneumothorax was induced there were 3 relatively large effusions, and in 3 cases there was a demonstrable quantity of fluid which did not increase or was subsequently resorbed. Webb, in Colorado Springs, reports "85 cases for pneumothorax in which we met with success more or less in the collapse of 63. Nine of these had moderately large effusions which we drew off part, and then they disappeared. I do not know how many we had with small effusions, as we did not Roentgen-ray them all." Shortle, of Albuquerque, New Mexico, reports "50 cases in which a satisfactory degree of compression was produced. Among these cases 9 developed an exudate, as shown by physical signs. No examinations of patients were made with

Roentgen-rays." We may take it then as probably true that on the high, dry plateau of the Rocky Mountains we do not have effusions in our pneumothorax cases with the frequency witnessed elsewhere, and when they do occur the tendency is to remain small and be reabsorbed. This phenomenon cannot be due to altitude, for von Muralt, at Davos, Switzerland, who has made a most exhaustive study of exudates, a report of which he presented last September before the eighth meeting of the Society of Sanatorium Physicians at Freiburg, states that at Davos they have the same percentage of exudates following artificial pneumothorax observed in other places. He observes without equivocation that general injury, such as cold, exertion, fatigue, intercurrent infections, account in a large measure for the occurrence of effusions. The reason why we do not apparently have quite so many effusions on the Rocky Mountain plateau may lie in the fact that we do not have colds and intercurrent infections among our tuberculous patients with anything like the frequency observed in less favorable climatic environments. It is only fair to observe, however, that in Europe this method has been employed much longer than in the United States, where it has only been used about three years to any extent, and that after longer experience we may see more effusions, though in the East the experience corresponds to that of Europe, even though they have employed pneumothorax a much shorter time.

Von Muralt, in common with most observers, thinks that the effusion in pneumothorax is directly parallel with the common exudative pleuritis; in other words, to use his exact language, "it is to be ascribed to a going over of the tuberculosis to the pleura." With this statement we do not wholly agree. The secretion of a fluid by the pleura is as natural a phenomenon as that of tears by the conjunctiva. If the tear duct is occluded the tears will overflow upon the cheeks. When the mechanism of the pleura is in perfect working order as to secretion and absorption an excess of fluid is never found; but we certainly know that as pneumothorax is protracted the absorption properties of the pleura become more and more impaired; that as time goes on refillings are required at longer and longer intervals, and in the presence of this impaired function on the part of the pleura it may be true that it will become less and less possible for it to take care of the excessive secretion. Exudate in the beginning may be a response to irritation, and the mechanical condition induced by pneumothorax, as well as a abnormal substance, such as nitrogen gas in contact with the pleura, certainly furnishes the factors of irritation. This theory will not apply to those exudates the result of pus infection, or of true tuberculosis of the pleura, in which tubercle bacilli are found in the exudate. However, these forms of exudate von Muralt states are in the minority, but we believe that this theory may be

the true explanation of the small serous and lymphocytic exudate. In contradiction to such a theory is the experience of Shortle, who has made it a practice to withdraw all exudates on their appearance in any quantity and replace with gas. It has been his observation after such a removal of exudate that it does not tend to return. Under our theory it would seem most likely to.

It has been proved that the choice of operation, whether Forlanini or Brauer, does not influence the occurrence of exudates. It also seems true that the more serious the case the more extensive the tuberculous pleuritis is or has been the more likely they are to occur. It is perhaps needless to say that the small and, as we think, mechanical effusions are of no importance and do not require treatment. In one of the four instances we have observed it was promptly resorbed, and in the three in which it persists there has been no tendency to increase. However, in the East and in Europe the large percentage of exudates observed becomes a factor of real importance in artificial pneumothorax. These exudates are said to gradually increase and more and more approximate pus in character, becoming first cloudy; later containing polymorphonuclear neutrophiles, and lastly tubercle bacilli. They finally lead to gross thickening of the pleura. It seems to be the common practice under such conditions and in the presence of pressure symptoms to remove a portion of the exudate and replace it with gas. All observers are practically a unit that washings and the injection of antiseptics are little worse than useless under these conditions.

We do not know when it first occurred to one of us, independent of artificial pneumothorax, in fact, years before we knew anything about this method, that nothing could be more favorable, especially in far-advanced tuberculosis, than an extensive effusion into the pleura. We are certain that independent of the practice of any other physician one of us (Bullock) distinctly conceived the idea that such effusions should never be disturbed except for pressure symptoms, and then only enough removed to relieve the circulation. Often after an effusion these patients would take on weight, present a normal temperature, slowing of the pulse, and a general feeling of well-being. The observation of a few of these cases in which effusion occurs naturally will prove to anyone that in such an exudate there is something, or a combination of things, which we suppose we can safely class under the generic term antibody or antibodies, which are vastly beneficial to the affected individual. There has never been a time during the past seventeen years when one of us has not had such a person under his observation, and we have a clear-cut conviction that as long as the fluid remains the individual is relatively safe, and that it is usually only upon its complete resorption that the tuberculosis resumes its course. As soon as Röhmer and Hamburger showed that the already tuberculous

animal could not be reinfected with tuberculosis, this, of course, being in line with Koch's original observation of the injection of tubercle bacilli into already tuberculous guinea-pigs, one of us (Bullock) felt safe in removing small portions of these natural effusions and injecting them into other and seriously ill consumptives. He did this several times, but to his surprise there was neither local nor general response. Why this fluid which partially protects the individual having it will not benefit others is difficult to understand. One reasonable explanation is, we think, that the quantity injected or possible of injection is too small or too infrequently employed, or both. The individual with the exudate, however, has a large reservoir of antibodies in the fluid upon which he can draw continuously.

Extensive exudates in artificial pneumothorax may produce, through vast pleural thickening, a marked shrinking of the pneumothorax, and, according to von Muralt and others, there occurs, in spite of refillings under high pressure, a retraction of the thorax with an expansion of the compressed lung before we are ready for any such functional mobility. Right here we must call in the surgeon and have him do a plastic operation, a Wehlm or some of its modifications, or better yet a Schede. We have never seen a pus infection of the pleura follow artificial pneumothorax. Such an accident must occur from infection from without by means of the needle or from perforation of the lung. All observers agree that they are very rare, and should be treated by thoracotomy, drainage, frequent washings, etc.

Von Muralt holds that on account of the great uniformity in the occurrence of pleural exudates in artificial pneumothorax that their cause must be wholly interior, and whatever the actual cause, whether a true tuberculous effusion (or, as we hold, the small mechanical effusion), he is undoubtedly right in attributing their causation to internal conditions and not to methods of procedure.

Von Muralt classifies the effusions as follows: (*a*) True serous or light sanguinolent exudates which remain small and show only a slight tendency to increase in quantity, and which generally disappear in the course of a few weeks or months. Of his 35 exudate cases 14 were in this category. Of our 5 exudates 4 were of this type (this is the character of exudate which we ascribe to mechanical causation). (*b*) Exudates which begin like (*a*) but have a greater inclination to increase and retain their character for a long time. (These also may be ascribed to a mechanical causation.) If, however, tubercle bacilli make their appearance in the effusion it is probable that a true tuberculous pleurisy has become superimposed upon the original effusion. As a rule, tubercle bacilli can only be demonstrated in these effusions by means of animal inoculations. Von Muralt has had 16 cases of this type which continued over a period of years, and in the later stages contained plentiful cell detritus. (*c*)

Virulent infections of the pleura with mixed organisms originating either through wound infection or rupture of the lung. Von Muralt has had 5 such cases. In one of our patients a natural was superimposed upon an artificial pneumothorax, with subsequent exudate, which examination proved to be sterile under the microscope. The fluid also proved negative when injected in a guinea-pig. Von Muralt makes it plain that the seriousness of the cases has a distinct influence upon the occurrence of an exudate. Of his 29 cases without exudate, 20 were moderately advanced, 7 very serious chronic, and 2 acute tuberculosis; while of his 35 exudate cases, 13 only belonged to the moderately serious class, 19 to the very serious chronic class, and 3 to the acute. With the first group exudates of the (*b*) type have been mostly observed by him. In his moderately serious cases exudate generally occurred later; in some cases not until a year after the first operation, and were usually small and serous. Von Muralt's experience corresponds to and may well be said to be a reflection of that of others. Therefore if it is so that the more serious the case the more likely the effusion is to occur it constitutes a most important reason for anticipating the use of pneumothorax and not waiting until the procedure is forced upon us. The microscopic examination of these exudates as well as animal experiments rarely shows anything, with the exception of the (*c*) type, but tubercle bacilli, if they are not wholly sterile, as is true of the (*a*) exudate.

According to von Muralt, Gratz, and Saugman it should be kept in mind that when a pneumothorax is present the pleura is unable to prevent a tuberculous focus from extending by means of the adhesion of the two membranes, parietal and enteral, but rather tuberculous foci are able to develop and spread on the surface of the pleura. The stimulation of such foci is in fact favored by tearing adhesions and stretching the pleura. In our opinion this accounts for some of the acute febrility manifested during the early stages of compression in some instances.

Saugman further states that we should remember that the pleura, through the steady contact with gas, is placed in a wholly unphysiological relation, which, as Kaufmann has demonstrated in dogs, produces an anatomical change of the serosa with a decreased ability of gas resorption, and as we would like to interject once more for the sake of emphasis, probably a decreased ability to absorb its own secretion. Von Muralt states that one has the right to accept the principle that the tuberculous pleura is particularly prone to exudative inflammation under these changed conditions. He also emphasizes that in addition to the causative factors already mentioned certain individual ones should be considered. In his 35 exudate cases, 11 had had marked pleuritis before the pneumothorax, and in these, in 6, exudate had occurred; to quote exactly, "doubtless, therefore, it is just the patients

which are individually disposed to exudates who take a pretty large share in pneumothorax exudates." Von Muralt, Forlanini, and Brauer all protest against the use of the term transudate as an explanation for the occurrence of fluid in pneumothorax. The reason for this seems to lie in the fact that the exudate does not appear in the beginning when the circulation changes are most marked. Faguoli, who has made a study of the character of exudates, has found them of not only high specific gravity, but with a high albumin content, which he states is good evidence in favor of their inflammatory origin.

Of course, on account of the extremely few exudates that have been observed in our work to date, it has been impossible for us to make any exhaustive study of their character; but in the 4 cases with small exudate that we have observed the exudate has been sterile even upon passage through animals. In the large exudate case the fluid is purulent and tubercle bacilli are present. For the same reason the insignificance of our exudate material, we are unable, from our own experience, to discuss the therapy of these exudates; notwithstanding which, as the result of a long and extended experience with natural exudates, we have very positive convictions regarding their treatment. From the point of view of treatment we can see no reason for differentiating natural effusions from those which follow artificial pneumothorax. We believe they should be handled the same, and that is, with certain qualifications to be explained later, let severely alone. If, however, upon gradual thickening of the pleura there is reëxpansion of the compressed lung before it is clinically desirable and by refilling with nitrogen it becomes impossible to prevent this premature expansion, or, as in some instances, even upon withdrawal of a portion of the fluid more nitrogen cannot be introduced, then, providing the patient is in a position to withstand the operation, the desirability of a plastic should at once be considered. Under these conditions our conviction would be that a Schede should be performed rather than the tentative and less complete procedure of Wehlm. Von Muralt and others agree that in the presence of inflammatory symptoms and an exudate that positive pressures cause more inconvenience than the same pressure previous to the appearance of the exudate. Under these conditions, lowering the pressure to zero may at once reduce the fever. This is in line with the observation that all of us should have made that there are patients without exudates who must always have a zero or a bit of negative pressure in order to be free from fever. It is well at this juncture to state pointedly tht every gas case is an individual matter, and that a theoretic degree of pneumothorax may practically prove undesirable. As one of us (Bullock) stated before the American Sanatorium Association in 1913, the least pressure that will accomplish the result clinically is the pressure to be maintained.

It now occurs to us that possibly one reason why we have seen so few effusions is because we have always used warmed nitrogen. The lack of this precaution may account in part at least not only for some of the effusions but also for the so-called pleural reflexes of which personally we have seen none. We have no doubt that von Muralt is correct in his observation that in small saculative, pocket-shaped, or indented pneumothorax, in which a compressing effect is only possible with high pressure, clots and progressive adhesions are easily formed. Several times we have been able to find a pocket which we could refill, using relatively high pressures, for a certain length of time, then, much to our surprise before we understood this phenomenon, we would never be able to find the pocket again. In such cases, if we are to accomplish anything with pneumothorax, high pressures and frequent refillings are essential.

It is advised in the presence of an exudate and inflammatory symptoms that the pressure should be kept neutral until the fever period is passed, high fever itself being treated by means of counter-irritation (the acutal cautery), the use of pyramidon, aspirin, etc. A small quantity of the fluid should be withdrawn for examination, and if pus and pyogenic organisms are found, energetic surgical measures should at once be instituted. If, however, the fever remains low in type we should employ all our supporting measures and patiently await an amelioration of the condition before resorting to radical surgical procedures. We will then have time to adequately study the situation, and if surgical intervention becomes necessary, know best just what sort of operation is likely to meet the situation. From von Muralt to Saugman and Brauer every observer is agreed that antiseptic injections into the exudate are worse than useless. In this connection von Muralt observes, in making his plea for the conservative management of exudates, that the removal of even a small portion of the exudate may exacerbate the symptoms. We have observed this phenomenon in natural effusions when we have been forced to remove a portion on account of pressure symptoms. In the absence of mixed infection in an exudate in which fever continues from one to two months or longer, von Muralt would not ascribe the fever to the exudate, but to a tuberculous focus either in the lungs or another organ. The same observation undoubtedly holds good in the absence of an exudate with the presence of a complete pneumothorax when fever persists.

All observers are agreed that in the presence of fever the removal of the exudate and cleansing of the pleural cavity—when the exudate has been sterile, or simply tuberculous and free from mixed infection—is more likely to accomplish harm than good. It should be remembered that it is in just such cases that with patience we are likely to witness the most happy sero-immunizing effect. To employ von Muralt's forceful observation, "whoever has been able to observe these remarkable beneficial changes will not do

things which do not bring any benefit anyway." In other words, to further follow von Muralt, the fact that an exudate is present does not indicate the use of surgery even if the test puncture looks ugly, grayish, and contains tubercle bacilli. He puts it very happily when he states "one must learn to consider the tuberculous pyopneumothorax as well as the dry pneumothorax as a pathological-physiological condition." When the temperature returns to normal in one of these exudate cases it is no longer necessary to keep the pressure low, and most observers are agreed that the individual indications can be followed as before the onset of the fever. It is as true of a large exudate as of a large pneumothorax that they may act unfavorably on the stomach, liver, and heart through the pressure exerted. Such conditions must be met either by lowering the pressure or partially removing the exudate. These large exudates are slowly resorbed, as is true in natural effusions, and the end result is the same in both instances, an enormous pleural thickening, which helps to permanently maintain the lung in a state of physiological rest. Nearly everyone who has to do with a large number of consumptives has observed this termination in natural effusions, and some of the most brilliant results in far-advanced cases we have ever seen have fallen in this category.

True empyemas with marked clinical manifestations are amenable only to plastic operations. Von Muralt thinks, however, that if they are small in quantity that large antiseptic injections, for instance, 20 to 30 c.c. electrargol in repeated doses, if necessary, are often sufficient to arrest the process. According to him this is particularly true of pneumococci infections. In his opinion, however, if improvement does not soon follow this measure, the exudates should be reduced through puncture; but the plastic operation for the reduction of the pleural cavity should not be done until the abscess has been drained by a thoracotomy, thus lessening the chance of infection of a large plastic wound. Forlanini states that the imposition of a natural pneumothorax upon an artificial one is an absolutely fatal catastrophe. We have had one such case in which all the classical symptoms of rupture of the lung were present, which were subsequently followed by an effusion of clear sterile serum, and in which instance up to the present time (eleven weeks after the rupture) the patient is either holding her own or improving a little.

A phenomenon which occurs in pneumothorax of very great interest, for it is still unaccounted for, is the preliminary marked loss of weight which occurs in many of these cases no matter how completely the clinical symptoms are relieved. We have endeavored to account for it specificially, but so far have had to content ourselves with the generalized explanation of altered metabolism and circulation following the unphysiological relations of artificial pneumothorax. It has been observed, however, that should effusion

occur the loss of weight stops promptly and the patient begins gaining in weight.

In this country it is too early to permit of adequate discussion of end-results. In Europe they are just beginning to do so, but it seems reasonable to expect that in time our end-results will approximate theirs. This will prove notably true providing the measure is reserved in the future, as it has been in the past, in large measure, for otherwise hopeless cases. If, however, as we advocate, the method is applied in all suitable cases that are progressive in type the story may read more happily. There is one point to be borne in mind which was especially marked in the experience of one of us in the earlier use of pneumothorax, and which we have not seen mentioned by other workers. It is this: It requires relatively a higher pressure and a larger pneumothorax to relieve the clinical manifestations in a lesion confined to one lobe than it does in more extensive disease of the lung. Under these conditions we more often observe the phenomenon which European operators designate as "puffing up of the mediastinum." In several instances in which we have performed this procedure in one-lobe cases we have had the physical signs and sounds of pneumothorax impinge upon the sound lung as much as three inches from only a slight positive pressure. On the reduction of such a pressure the former signs and sounds returned to the area in question. We have never seen any harm come from such a dislocation of the mediastinum.

For many years the workers in the Rocky Mountain plateau have tried to impress upon their Eastern confrères that under our climatic conditions the picture of tuberculosis is altered and ameliorated as compared with the manifestations of the disease in many other localities; that patients do not have night sweats; that hemorrhages are less often observed; that fever is less often in evidence, and patients apparently acquire sooner, and in greater number of cases, a toxic immunity; that the circulation is improved; that the red blood cells are increased in number; that the percentage of lymphocytes tends to increase; that tubercle bacilli disappear sooner from the sputum; that the lesions are drier; and, in fact, that we get better results. We would furthermore like to impress upon our Eastern confrères that we apparently do not have exudates, or such serious exudates, with the same frequency as they do in the East and many other localities.

PELLAGRA IN CHILDHOOD.[1]

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Pellagra was first described by the Spanish physician Casal in 1735, although Frapolli gave the appellation to the affection in 1578. The importance of the disease cannot be overestimated, as in the year 1884 Italy reported the appalling total of 104,067 cases, which fortunately decreased to 60,000 in 1903, and since then has exhibited a still further abatement. Our own country is showing an increased epidemic, since the disease is becoming more generally recognized, particularly by the physicians of the South. C. H. Lavinder made the calculation that from 1907 to 1911 a total of 25,545 cases of this affection were observed in the United States; 15,870 of these occurred in the States of North Carolina, South Carolina, Georgia, Kentucky, Alabama, Mississippi, and Louisiana. The Northern States have been afflicted with comparatively few cases, and therefore those of us who have desired to study the affection have been compelled to visit the neighborhoods where the disease is endemic.

During the last four years I have had the opportunity of studying about a dozen cases of this affection in Philadelphia and in the neighborhood of forty in the South and Southwest. Two of the cases observed in Philadelphia occurred in childhood, one of which has already been reported by Dr. Hartzell. Although very little has been written exclusively on pellagra in childhood, the further one delves into the disease the greater becomes the conviction of the frequency of this affection in children.

Age. Lavinder found in a statistical study of 15,870 cases of pellagra, 412 under five years of age and 1719 between the fifth and twentieth year. Merk tabulated 4836 cases of the affection, of which 46 were observed under five years of age (0.9 per cent.) and 406 between the fifth and fifteenth year (8.3 per cent.). R. M. Grimm made a study of 323 cases from Kentucky (three counties), South Carolina (seven counties), and Georgia (fifteen counties) and discovered 15 cases under five years of age, 23 from the fifth to the tenth year and 23 aged ten to fifteen years. Sambon states that pellagra is quite a frequent occurrence in children, particularly after two years of age. There have been, according to Rohrer, 31 cases of this affection in Maryland up to September 25, 1912, 4 of which occurred in children aged six, nine, ten, and eleven years respectively. Mizell observed 15 cases of this affection under fifteen years of age out of a total of 100 cases. Potarca collected

[1] Read before the Philadelphia Pediatric Society, January 12, 1914.

17,027 cases of pellagra and found 13 per cent. under twenty years of age. Calderini, in Italy, observed, in 1844, 352 cases of this affection and found 83 of them under three years of age. Siler and Garrison discovered in a series of 254 cases, 21 under six years of age, 22 from six to nine years, and 28 from ten to nineteen years. Mason has seen 20 instances of the affection under the age of twelve years. Snyder sent a circular letter to sixty physicians of the South who had had extensive experience with pellagra and the consensus of their replies placed the prevalence of the disease in childhood at 10.5 per cent.

According to Snyder the youngest case observed by any of these sixty physicians developed at the age of two months (Savage). Chrisoferetti records instances of the affection at forty days, five, seven, ten, and seventeen months respectively. Sambon has seen cases at three, four, and five months, and states that while such early cases are rare the disease is quite frequent in children from six to eighteen months. The latter considers puberty in boys a vulnerable time for the pellagrous attack. Roberts has studied 2 cases of the affection at the age of four and five months respectively.

Sex. It is a well-known fact that the female sex in the adult is very much more apt to be attacked than are males. Siler and Garrison found in a study of 282 cases there were 191 females showing the affection and but 66 males. They found from one to six years of age, ten males and eleven females attacked, and from six to eleven years, twelve males and the same number of females. Rohrer reported that 3 out of 4 cases under fifteen years of age attacked by pellagra were of the male sex. Mizell recorded 15 cases under fifteen years of age, 5 were females and 10 males. Of 85 cases of this affection seen by Rice in two orphanages, 45 were females and 40 males. Tucker recorded 4 cases under fifteen years of age, 3 were males and 1 a female.

Race. Lavinder analyzed the sex and the race in 15,870 cases without separating the adult and the childhood cases. He found in the white race 2924 males attacked and 6857 females, and in the negroes, males, 931, females, 3117. Siler and Garrison compared the frequency of attack in the white and negro races. They found in the community where pellagra was endemic out of 282 cases, 257 occurred in the white race while but 25 were found in negroes; of these 25 cases but 1 was observed under six years of age, 1 also between the sixth and the tenth years.

Pellagra in Families. Sambon makes the statement that in families with numerous children living in districts where pellagra is endemic he has often found the parents and all of the children attacked. Siler and Garrison report that in one-half of the cases observed the disease occurred singly in one family, about one-quarter were noted two in one family, and the remaining one-quarter in groups of three, four, or five in one family.

PRECEDED OR ASSOCIATED WITH OTHER DISEASES. Of the 43 cases observed by Siler and Garrison, infantile paralysis preceded the pellagra in one instance, chicken-pox in another, and whooping-cough in two others. Measles occurred before the pellagrous outbreak in 12 instances; 11 of these were under twelve years of age (approximately 23 per cent.). In most of these the attack of pellagra occurred shortly after recovery from measles (Siler and Garrison). Sambon recorded a case in a child of three years which developed shortly after an attack of pneumonia.

Because of the frequent occurrence of hookworm in the South the association of this affection with pellagra is often observed. Rice in order to determine the relative frequency of hookworm in the pellagrous and the non-pellagrous examined microscopically the stools of all the inmates of an orphanage and found that 26 per cent. of the total population were infected. Hookworm was found in association with pellagra in 29 per cent. of the cases.

DIFFERENCES IN SYMPTOMATOLOGY BETWEEN THE ADULT AND THE CHILD PELLAGRIN. *Cutaneous Manifestations.* Snyder found in his investigations that the skin outbreak in children was more prominent than the other manifestations of the disease. According to Wood, children, as a rule, are not seriously affected, the cutaneous outbreak being the most prominent feature. Sambon believes the malady is frequently overlooked in childhood because it is often very mild and of a short duration; the parents not infrequently believe their children only sunburnt.

In the cases observed by Rice in the orphanages of the South all of the eruptions were of a dry type, usually on the dorsum of the hands and the feet, in some only on the former; in certain instances extending up the backs of the legs, some only on the backs of the forearms and calves. He found the covered portions of the body attacked in but two instances; a mask form was present in one instance; Casal's necklace in one case; and the face and the neck were involved in a few. After desquamation in these cases the affected surface was smooth and of a lighter color than the adjacent unaffected skin. A few complained of burning of the affected areas. Thirty-three of his 43 cases had the dermatitis on the dorsa of the feet and the calves of the legs; these were the barefooted children. In the larger children who wore shoes the dermatitis was on the backs of the hands alone or the backs of the hands and the forearms.

Merk analyzed, in children and adults, 1679 cases of pellagra; 77 per cent. had an erythema on the backs of the hands alone; 282 cases (13 per cent.) had the eruption on the backs of the hands and the neck; 164 (7.5 per cent.) had the outbreak on the neck; 53 (2.4 per cent.) had the dermatitis on other portions of the body. In only 5 per cent. of Wood's 189 cases were the lesions lacking on the backs of the hands, and most of these patients were children

who were accustomed to go without shoes and stockings, thus exposing these areas as much as the hands.

Gastro-intestinal Symptoms. Rice in a study of 43 pellagrous children found that 16 had frank sore mouth, 8 had diarrhea, and 22 a denuded and fissured tongue. The mucous membrane of the mouth was redder than normal, but did not have that fiery redness which is seen in the severe types of the disease. Some had "geographical" tongue.

Nervous System. Rice found but few changes in the nervous system in his series of pellagrous cases with the exception of the patellar reflexes. In 54 cases in children he found the reflexes exaggerated in 28; decreased in 10; absent in 6; normal in 8; and unequal on the two sides in 2. Snyder found after comparing his statistics with fifteen other authorities on the subject that the nervous manifestations of the disease were very much less marked in childhood than in adults. Such also was the experience of Mason in his 20 cases in children.

Other Manifestations. The hair is not usually affected in those developing pellagra during adult life, but in children it is often short, thick, and course, lacking the usual amount of sebaceous matter, and feels rough (Roberts).

Comparative studies of the blood findings in adults and children with the disease have not been made in a sufficient number of cases to determine the resemblance or difference. In a considerable number of these cases there is some anemia present; the small lymphocytes are relatively increased, and the large mononuclear cells normal or diminished in number.

Indicanuria is very common and oftentimes a constant accompaniment of pellagra. Rice found in 42 cases of pellagra in children an excessive amount of indican in the urine in 50 per cent. of those attacked. The interval between the active attacks gave the reaction as markedly as during the stage of activity.

Rice made a comparative study of pellagrous and non-pellagrous children and found, at the same age, they were approximately the same weight and height. A large proportion of those attacked seemed to be in excellent physical condition.

Etiology. The conflicting views on the cause of the condition will not be discussed in the present article, with the exception of the question of heredity.

Snyder received eleven replies to his interrogation upon this phase of the subject; 9 had seen pellagrous mothers who had been or were nursing infants without any manifestations of pellagra being present in the latter; 13 babies were represented. None of Grimm's observations have led him to believe that the affection is hereditary. The latter reported 58 children whose mothers had developed pellagra within one year after the birth of the child, 9 were dead (cause undetermined) but none was pellagrous; of 18

children whose mothers had developed the disease within one year before the birth of the child, 2 were dead but none of the living were pellagrous. Grimm found that of 30 infants who were being nursed by pellagrous mothers, none were pellagrous at the time of his visits, 6 were not well, and 24 were healthy.

According to Sambon, he has never seen or heard of a single case of congenital pellagra, neither has he been able to find in literature any first-hand and authentic record of a case. Roberts states that pellagra is not inherited, but the ravages in the parent is inherited and appears in the child in the form of dwarfism, deficient development, anemia, various malformations of the skull, asymmetry, badly set ears, mental weakness, slow growth, an unusual lack of resistance, and a frailness out of all proportion to the age. Boudin prepared a paper on this phase of the subject: The first three groups with pellagrous parents give 443 pellagrous children, while the last two groups with the parents well give 297 pellagrous children; an excess in favor of pellagrous degeneracy and predisposition of only 20 per cent.

Agostini believes that the disease is not inherited, but that a certain weakness is present which makes the affection more easily acquired and tends toward the "gravest syndrome of somatophysical degeneration such as dystrophic cretinoid and myxedematous infantilism."

Case Report. Harry E., aged five years, came to the skin dispensary of the Children's Hospital July 10, 1914, because of an eruption on the face and the hands. A marginated dermatitis, dull red in color, was observed on the hands, ending abruptly at the sleeve line, and on the face extending half-way up the forehead to the hat margin. The same condition was noted on the rims of the ears. He has had several attacks of this dermatitis, beginning in the early spring and extending during the summer. Its occurrence is apparently independent of sunlight. The face is more or less red even in winter, but much less so than during the spring and the summer; desquamation of the affected areas occurs several times during each of the latter periods.

The tongue is partially denuded of mucous membrane and quite red. Other portions of the mouth likewise show this redness. The bowels move on an average of three times daily, usually after meals. The patient is quite thin, very small for his age, and is exceedingly nervous. The knee-jerks are diminished, the gait sluggish, incoordination poor, speech hesitating, pupillary reaction lessened, and there is a decided hebetude. His gait is decidedly ataxic, walking like a child with spastic paraplegia of the toxic multiple neuritis type. The urine examination was negative excepting for an excessive amount of indican.

During the two months the case was under observation the eruption became of a typical dark brown, mahogany color, and exfoli-

ated, leaving the skin dry and atrophied. The diarrhea continued and the nervous symptoms remained the same. The history insofar as it is obtainable apparently shows an attack of infantile paralysis; shortly afterward the present symptoms developed. The gastro-intestinal symptoms started at six months of age; the dermatitis appeared shortly afterward. The mother is healthy while the father has always been delicate, and is an inveterate cigarette smoker. The mother was born in Italy while the father is Irish. The child has always lived in the suburban portion of the city. While the case was under observation, quinin, salol, and mercury and chalk were given internally. The child when last seen was in much the same condition as when he originally came under observation, excepting that the active dermatitis was not present, as it was in the autumn.

Prognosis. Lavinder found the death rate in 15,870 cases of pellagra between the years 1907 and 1911 was 39.1 per cent., both adults and children being represented in these figures. Rice records 103 cases in children from 1907 to 1913, and but three deaths have occurred during this period. Snyder found that nineteen other authorities on pellagra considered the mortality in children either much less or less than in adults. The two cases I have seen in children one is dead and the other is still living.

In conclusion I wish to emphasize the importance of the pellagrous eruption. In communities where very few cases of pellagra are seen there seems to be a distinct tendency to diagnose every symmetrical eruption as a case of this disease. The color of the eruption should be particularly emphasized; a marginated, symmetrical dermatitis of the exposed parts of a deep mahogany shade, as if the skin had been painted with iodin, could scarcely be mistaken for any other affection, particularly if associated with gastro-intestinal and nervous symptoms. A considerable amount has been written on pellagra without eruption, "pellagra sine pellagra."

A paper on this disease could scarcely have a better ending than to quote two recent articles: Roussel, who first employed the term "pellagra sine pellagra," states: "The expression pellagra sine pellagra can only be applied to a temporary absence of the cutaneous eruption, either at the beginning or during the course of the malady."

Siler and Garrison start their instructive paper, "An Intensive Study of the Epidemiology of Pellagra," with the statement, "In view of the essential importance of diagnosis in our work the conservative position was taken that a positive diagnosis would be made only when the characteristic skin lesion was evident or its earlier presence could be definitely ascertained by the testimony of patient and physician."

Conclusions. Pellagra is of rather frequent occurrence in childhood. In endemic neighborhoods approximately 10 per cent.

of the cases occur in children. The disease is rare under two years of age.

The affection is almost evenly divided between the two sexes in childhood.

The negro is far less susceptible to the disease than is the white individual, particularly in early life.

In endemic neighborhoods in about one-half of the cases two or more members of one family are attacked (Siler and Garrison).

In a considerable number of cases in children, pellagra follows shortly after the exanthemata, particularly measles. In the South, pellagra in children frequently develops in those with hookworm.

The skin eruption in childhood is quite marked, while in a considerable proportion of cases the gastro-intestinal and nervous symptoms, particularly the latter, are comparatively mild.

Although formerly the death rate in children was rather high, at present, the disease occurs in a much milder form and the mortality is low.

Heredity plays no part in pellagra, excepting by lowering the general resistance of the child, the disease is more readily contracted.

The typical cutaneous outbreak or an accurate history of its former occurrence is essential in making the correct diagnosis of pellagra.

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THE BORDERLAND BETWEEN MEDICINE AND SURGERY IN RELATION TO CHRONIC PROSTATITIS.[1]

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Chronic inflammation of the prostate gland is one of the commonest diseases with which the adult male is afflicted. Out of approximately 500 adult men seen by the writer in medical practice, 36, or 7 per cent., were suffering from this disease. Chronic prostatitis is often overlooked, particularly when the symptoms do not point directly to the pelvic organs as the possible site of trouble; yet many symptom-complexes depend directly upon this condition, and their cure is well-nigh impossible without recognition and treatment of the primary prostatic disturbance.

This paper is not intended to be a treatise upon chronic gonorrhea, but to take up briefly a class of cases which presents general medical symptoms, particularly of a nervous character, caused by inflammation of the prostate gland. This may in turn depend upon a previous gonorrhea, perhaps long forgotten, or may have been induced by other causes. In discussing this subject I wish at the outset to express my great debt to the late Dr. Nathan Jacobson. Through his influence I was led to take an interest in this branch of medicine, his knowledge of which far exceeded that of any physician or surgeon I have ever known. The cases upon which this study is based are taken largely from Dr. Jacobson's records, partly from my own.

The normal prostate gland resembles a horse-chestnut in size and shape. It lies just below the neck of the bladder, and is penetrated from base to apex by the prostatic urethra. The structure of the prostate is comparatively simple, consisting of a connective-tissue capsule, from the inner aspect of which numerous muscular and connective-tissue bands run inward to form the stroma of the organ. In the interstices of the stroma, and supported by it, lie the prostatic glands. They are of the compound tubular type, and end in ducts which empty by fifteen or twenty openings into the prostatic urethra along the sides of the veru montanum. The two ejaculatory ducts pass through the substance of the prostate and empty upon the summit of the veru montanum, a small but important muscular structure which forms part of the floor of the prostatic urethra.

The prostate gland is provided with a free blood supply, and is surrounded by a plexus of veins so large and so closely interwoven

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as to suggest the cavernous spaces of an erectile tissue. The veins of the prostate form one of the connecting links between the portal and inferior caval systems. The nerve supply shows an extraordinary wealth of nerve fibers, ganglion cells, and nerve end-organs. It is conceivable that the unusually rich blood and nerve supply of the prostate may determine on the one hand the readiness with which the gland undergoes congestive changes, and on the other hand the numerous local and general nervous manifestations associated with prostatic inflammation.

After studying the structure of the normal prostate it becomes easy to understand some of the changes which chronic inflammation brings about. If, for example, there is an increase of the connective tissue sufficient to compress some of the numerous tiny ducts the secretion of the tubular glands becomes dammed back, dilatation of the glands follows, and often small cysts are formed. The inflammatory changes may involve principally the stroma which increases in density, thereby producing a hard prostate, or the glandular structures may bear the brunt of the inflammatory changes and become distended with purulent secretion. In the latter instance an enlarged but soft or adenomatous prostate results. As a rule, both the glands and the interstitial tissue are involved, although often in unequal degree. Cases of long standing with much sclerosis show contraction or even obliteration of many glands.

The most common cause of chronic prostatitis is, of course, gonorrhea. "For practical purposes," as Hugh Cabot says, "chronic gonorrhea is chronic posterior urethritis, and in the same way chronic posterior urethritis is chronic prostatitis." Inasmuch as the posterior urethra is probably involved in from 70 to 90 per cent. of all cases of gonorrhea, it goes without saying that chronic gonorrheal prostatitis must be a very common disease. It is not so generally recognized that there is an important class of cases in which chronic prostatitis exists with no antecedent gonorrhea. The etiology of non-gonorrheal prostatitis is not entirely clear. Young believes that the prostatitis is of bacterial origin and that the organisms are probably conveyed to the prostate by the blood stream or from contiguous structures, notably the rectum. Of underlying factors the most important appear to be prolonged sexual excitement without gratification; excessive masturbation or sexual intercourse; irregular sexual practices, as coitus interruptus; and occasionally bicycle- or horseback-riding. Lydston states that when the periods of rest between the acts of ejaculation are so short that the circulation cannot regain its normal equilibrium, disturbances of the prostate are likely to follow. He considers that any masturbator who has practised the habit for any considerable length of time may be regarded as having a more or less swollen and tender prostate. Keyes lays stress upon cases where

there is association with a person of the opposite sex who permits dallying, even though coitus is not indulged in, thereby producing excessive dilatation of the prostatic vessels. Any or all of the above-mentioned factors probably pave the way for later bacterial invasion.

The symptomatology of chronic prostatitis is exceedingly varied, and, as Young says, may involve any of the organs in the various regions between the diaphragm and the toes. Pain is one of the most common complaints, usually dull and aching in character. It may involve the abdomen, back, external genitals, rectum, perineum, or be referred down the legs even to the toes. Among the conditions simulated may be renal calculus, lumbago, varicocele, sciatica, disorders of the abdominal viscera, and neurasthenia. Young has reported a number of cases in which there was strong resemblance to renal colic, even to the appearance of blood in the urine. In some instances the symptoms very closely simulate those of prostatic hypertrophy. Here it is exceedingly important to recognize the true condition, as proper treatment will save the patient from catheter life or an operation. McCrae mentions cardiac symptoms, such as anginal pains, palpitation, and tachycardia, accompanied by feelings of anxiety and distress. A common complaint is a sensation of fulness just within the anus, even though the rectum may be entirely clear of feces. With reference to urination there may be pain before, during, or after the passage of urine, or inability to expel the last drops of urine. Among the sexual symptoms may be mentioned diminution or loss of sexual power, premature ejaculations, and nocturnal pollutions.

The mental effects of chronic prostatitis are of great importance. Dercum states that there is apt to be difficulty in the performance of mental acts which require concentration, and a distinct disinclination for mental work. The sleep is often distrubed and true insomnia may result. The well-known picture of sexual neurasthenia or hypochondria is familiar to all. The patient has his mind constantly fixed on his sexual organs, believes that he is afflicted with severe or incurable maladies, and falls a ready prey to the quack, who knows best how to play alternately upon his hopes and fears.

The diagnosis of these conditions is simple. It depends upon rectal touch and the examination of the expressed prostatic secretion. The prostate usually feels enlarged, and may be irregular and indurated, or soft and boggy. Often it is nodular or shotty, due to dilated or cystic glands, and in many cases areas of softening and infiltration are irregularly encountered over the surface of the gland. Old inflammatory adhesions may extend from the prostate to the sides of the pelvis, making the organ more fixed than normal, and usually involving the seminal vesicles, with obliteration of the furrow between the upper margin of the prostate and each seminal

vesicle. Inflammatory changes in the substance of the vesicles may coexist. Tenderness of the prostate is frequently met with, and in some cases the patients can hardly endure the lightest touch.

Normal prostatic secretion is a thin, milky fluid containing principally lecithin bodies (round, refractile structures the size of a red blood cell), granular phosphates, mucus and an occasional leukocyte, epithelial cell or amyloid body. In chronic prostatitis the secretion is increased in amount, and is yellow and thick. Occasionally it is tinged with blood. The characteristic feature of the microscopic examination is the presence of pus. Young states that in some cases pus is not found at the first examination, and the prostate may have to be massaged several times before pus appears. This, however, is not the usual occurrence. The amount of pus gives a rough estimate of the degree of inflammation. In cases which are progressing toward cure the polynuclear cells are gradully replaced by mononuclear elements. The constant absence of pus excludes active prostatic inflammation.

Investigation of the expressed secretion for bacteria is of some assistance. The finding of the gonococcus, of course, gives positive information, but as most of the cases are of long standing this organism is either very hard to find or has entirely died out, its place being taken by secondary invaders. Occasionally cases are reported in which the gonococcus has persisted in the prostate for a great many years, but many competent observers believe that it is exceptional for the organism to be found after three years. In the non-gonorrheal cases various bacteria have been encountered, such as the staphylococcus, streptococcus, or colon bacillus.

Inflammatory changes in the posterior urethra usually accompany prostatitis, and particularly affect the veru montanum or colliculus seminalis. Expert endoscopic examination is likely to reveal congestion, infiltration, or enlargement of this structure, with perhaps dilatation of the ejaculatory ducts. In many cases the prostatic urethra is extremely hyperesthetic.

The sheet-anchor of treatment is prostatic massage. Although a simple procedure, it is one that requires a considerable degree of skill when scientifically performed. The patient stands with his legs apart, the knees held stiff, and the trunk bent well forward. The physician is seated behind the patient and rests the elbow of the examining hand against his thigh for additional leverage. If preferred he may stand with one foot upon the seat of a chair and the elbow resting against his knee. In some cases it is necessary to press very firmly against the perineum in order to reach the upper part of the prostate. The free hand of the examiner may exert counterpressure over the lower abdomen if this is needed. The gland should be methodically and slowly stroked from above downward and inward, and the entire organ systematically covered. Two or three minutes are usually sufficient. Haphazard rubbing

of the rectal mucosa is to be avoided. At the first treatment it is well to err upon the side of gentleness, as with some patients massage seems to produce powerful reflex effects. They become pale and faint and are covered with profuse perspiration. At subsequent treatments the degree of pressure used can be gradually increased. It is desirable for the patient to have the bladder moderately full of urine or, perhaps even better, for the physician to distend it with a mildly antiseptic solution. Failure to observe this precaution is said to occasionally result in infection of the urethra from the expressed prostatic secretion, although in our experience this has never occurred. In case no glove is worn on the examining hand, but only a finger-cot, additional protection is afforded by thrusting the finger through a small opening in the centre of a piece of gauze eight inches square. The value of prostatic massage lies in periodically emptying the dilated prostatic tubules of their retained secretion, and in promoting absorption of the inflammatory infiltration of the prostatic tissue. Ordinarily it should not be repeated oftener than once in three to five days, the latter interval usually being the most satisfactory.

Instillations into the posterior urethra by means of a drop syringe are often very helpful in overcoming the associated posterior urethral inflammation or irritability. We have had the best results with a 30 per cent. solution of Argyrol. In some cases hot or cold rectal irrigations with a two-way rectal tube help to stimulate the gland and promote resolution. In suitable cases additional urethral instrumentation may be needed, such as irrigations, dilatations, the passage of sounds, etc.

Every effort should be made to improve the patients' general health, and various tonics and sedatives may be needed. Sometimes, in intractable cases, a complete change of scene, with suspension of all treatment, will bring about a cure. Psychotherapy should not be forgotten. Most of these patients are introspective, and have a tendency to magnify their symptoms. Many of them become discouraged at the length of time necessary for cure. It is only too true that the most important element in the treatment of chronic prostatitis is time, and the longer treatment is continued the better are the chances of cure. An absolute anatomical cure can never be expected, as the pathological changes in the gland are usually too far-reaching for complete resolution, but a symptomatic cure can, as a rule, be obtained.

This paper is based upon the analysis of 161 cases of chronic prostatitis seen during the past twelve years. Of this number 100, or 62 per cent., gave a history or other evidence of the presence of gonorrhea; 61 cases, or 38 per cent., gave no history of gonorrhea. Even granting that a few of the patients may have been unwilling to admit a previous venereal infection the proportion of non-gonorrheal cases, fully one-third, is fairly large.

CASE I.—*Close simulation of lumbago; relief afforded by prostatic treatment.* J. M., aged forty-six years, miller, seen February 2, 1903. Denies venereal disease. Nearly a year ago was seized with a "crick in the back." At first it was intermittent, lately it has become constant. At times he cannot bend his back. The pain affects principally the lumbosacral region. He has been treated by cauterization of the back and also by static electricity.

The prostate was found to be enormously congested, and after massage there was a very free discharge of prostatic secretion. Treatment by prostatic massage was continued at irregular intervals for two months. The prostate became much reduced in size and scarcely any discharge appeared after massage. The pain in the back disappeared save at rare intervals and the patient felt greatly improved in strength and vigor.

CASE II.—*Symptoms suggesting prostatic hypertrophy; patient saved from catheter life by treatment of neglected prostatitis.* C. V. W., aged sixty-two years, manufacturer in metal trade, married, seen September 21, 1907. Patient had a mild attack of gonorrhea about forty years ago, and syphilis thirty or thirty-five years ago. Four or five years ago he began to have painful urination. The pain seemed to come on when the bladder was full of urine and persisted until urine was passed. At first the desire to urinate was not very pressing, but during the past year he has had periods of marked disturbance. As a rule, he urinates five or six times a day, and until lately has not been up at night. These periods of aggravation of the trouble recur every two or three months, and last four or five days. At such times he is obliged to urinate every two hours and the desire to pass urine during the time is increased. For the past three or four days he has urinated more frequently than usual. He is up three or four times at night and has distress at the end of urination. The urine is clear and he has never passed any blood. At no time has there been retention. A physician advised him to use a catheter, and he has done so for four or five days.

Examination showed the right lobe of the prostate to be sensitive and much larger than the left; both were of soft consistency and easily reduced by massage. Three ounces of residual urine were found in the bladder. At the end of two and a half months' treatment the prostate had lost its tenderness and was nearly normal in size. The patient experienced marked relief from symptoms, was able to sleep all night in comfort, and had no disturbance of urination by day.

CASE III.—*Urinary symptoms depending upon old gonorrheal prostatitis.* V. K., aged forty-seven years, tailor, married, seen February 28, 1907. Patient denies venereal disease, but in 1890 had an internal urethrotomy performed for stricture. Five or six years ago he began to suffer from burning during urination and a sense of pinching of the bladder. As soon as the urine enters

the bladder there is a desire to urinate. This desire begins to manifest itself within fifteen minutes after he has emptied his bladder. He is then in great distress until he can void urine. The longest period that he can hold it is one and a half hours. At night he does not awaken until five in the morning, and is then obliged to urinate several times in succession. He feels the irritation and pressure mostly at the head of the penis. The bladder holds, he thinks, about three ounces. He is very comfortable after urinating. If he holds the urine too long it is apt to dribble away.

The prostate was normal to touch, but the right seminal vesicle was tender. Upon massaging the prostate a gleety discharge occurred which contained gonococci. No evidence of urethral stricture or bladder stone was found.

Treatment.—Prostatic massage, with deep urethral injections of 2 per cent. silver nitrate solution at five-day intervals, tonics, urinary sedatives, and antiseptics. Improvement began almost immediately, and at the end of ten months the urinary symptoms had almost completely disappeared. The patient was able to hold his urine many hours by day, was not disturbed at night, and felt stronger and better in every way.

CASE IV.—*Unusual sexual symptoms depending upon chronic prostatitis.* T. D., aged sixty-five years, miller, seen February 17, 1906. Denies venereal disease. Has been married twice. Prior to his first marriage he suffered a great deal from seminal emissions. During the early years of his first marriage he did not have proper control of his sexual organs during intercourse, but of late there has been no trouble in this direction. For a period of several years he has been awakened at night, from one to three or four times a week, with a series of painful erections. Each time it is associated with an urgent desire to urinate. Sometimes this occurs four or five times a night. The next day he feels completely tired out. He suffers from a feeling of pressure and bearing down in the left side of his scrotum and over his left hip. Other nights he is apt to be awakened two or three times to urinate. During the day he urinates about four times. He is apt to urinate oftener on the days following the erotic nights. He never has had any failure of sexual power, but feels nervous and broken down in health.

The prostate was found to be moderately enlarged, soft, and easily reduced by pressure. Two drachms of residual urine were present. The patient was somewhat improved by repetition of the massage, but did not come regularly for treatment.

CASE V.—*Headaches induced by sexual intercourse, and caused by chronic prostatitis.* R. R., aged forty-five years, farmer, married, seen April 1, 1911. Two and a half years ago he had an obstinate attack of gonorrhea. A year ago he began to have attacks of pain in the forehead and back of his head, lasting about twenty-four

hours. Each time the attacks would be brought on by sexual intercourse. While engaged in the act he would be seized with intense pain in the back of his head, which would extend to the forehead. These seizures do not occur every time he has intercourse, but have become more frequent of late.

The urethra was found to be very sensitive, and the prostate exceedingly tender, enlarged, and soft, with greater involvement of the right lobe. Under massage it was considerably reduced in size.

Treatment consisted of prostatic massage, instillations of Argyrol into the prostatic urethra, and suitable medication. The patient was advised to abstain from sexual intercourse as much as possible. He was under observation for two and a half months, and showed great improvement. The attacks of pain during intercourse entirely disappeared, his sexual vigor became greater than for many years past, and his general condition decidedly better.

CASE VI.—*Sexual neurasthenia relieved by treatment of the prostate and urethra.* M. M., aged thirty-nine years, married, railway mail clerk, seen June 8, 1910. Patient had gonorrhea twelve years ago and again three years ago. For several years has worried excessively over trifles. Six months ago he had an attack in which he began to tremble and felt as if he would collapse. He has had frequent spells of this kind since. For three months has been troubled with insomnia. He has what he calls shivers and seems to tremble inside. He is weak and tired and has pains in the heels after standing. Blood rushes to the head at times and there is ringing in the ears. He is particularly anxious about his sexual organs and his mind is constantly occupied with sexual matters. The patient admits excessive indulgence in sexual intercourse, but states that of late his sexual vigor has diminished and he fears that he is losing his vitality. After urinating he frequently feels as if he had not fully emptied his bladder, and there is apt to be a stinging sensation with some dribbling of urine.

Nothing abnormal was found in the urethra, but it was exceedingly sensitive to the passage of a sound. The prostate was very large, and after massage there appeared a great quantity of mucopurulent secretion streaked with blood.

The patient was under observation for over a year and was treated by massage of the prostate, the passage of sounds, and suitable internal medication. The urethral sensitiveness entirely disappeared, but when last seen the prostate was still large and considerable secretion could be expelled by massage. The symptomatic improvement, however, was very marked. The numerous nervous manifestations largely disappeared. The insomnia was replaced by restful sleep, the sexual life became more nearly normal, and the ability to do better work and to enjoy life were greatly increased.

CASE VII.—*Sexual hyperesthesia causing excessive sexual excitement.* H. M., aged thirty-two years, married, seen July 3, 1911. Patient never has had any definite illness. States that he began to masturbate when he wore dresses, and has always been exceedingly passionate. For years his sexual desire has been most violent, and he sometimes has intercourse with his wife as many as six or eight times in a single night. He is thoroughly aroused over his condition and tries very hard to control himself, but seems unable to do so. He is very nervous and has a great deal of indigestion. He has pain in the back and a feeling of irritability in the rectum.

The prostate was found to be greatly enlarged and soft. A large quantity of prostatic secretion was forced out by massage. Immediately the patient had a series of hysterical convulsions. He jerked, twitched, and was greatly agitated. He afterward stated that many years ago he had been similarly affected by having sexual intercourse. After three and a half weeks of treatment by prostatic massage an attempt was made to pass a sound, but the mere introduction of it into the meatus again threw him into convulsions. The influence of massage, however, was little short of wonderful. The nervous symptoms showed great improvement, the stormy sexual desires lessened, and after a time he could endure the passage of a sound without difficulty.

In this case the excessive masturbation of early life probably led to congestion of the prostate, which was later followed by true prostatitis. The inflamed prostate still further stimulated the patient's sexual desires, which were always unduly strong, until relief was obtained by suitable treatment.

CASE VIII.—*Painful seizures of obscure origin; stone suspected; relief afforded by treatment of the prostate and deep urethra.* J. M., aged fifty years, druggist, seen April 30, 1912. Patient never had any acute illness, although he has never been vigorous. Ten years ago he broke down nervously, and since then his power of endurance has been much diminished. Two years ago he was taken with pain to the left of the navel, which extended into the groin. The next day he vomited and had a continuance of the pain. Three weeks later he had a similar attack of pain which extended to the end of the penis and up his left side into the back. For a year he had recurring seizures of pain about every three weeks. He never passed any gravel. Roentgen-ray examination for stone was negative. The urinary tract was carefully investigated on several occasions, including ureteral catheterization, but nothing abnormal was found save a small swelling on the veru montanum. This was treated with silver nitrate and the patient had no attack of pain for a whole year. Lately he has had a constant desire to urinate and an uncomfortable feeling after urinating. The pain extends to the head of the penis, but if his bowels move freely the pain disappears. He complains of smarting in the perineum, with

pain in the right groin and right hip. For the past week he has had pain shooting up and down the penis, and the desire to urinate has been very urgent.

The prostate was found to be considerably enlarged, especially the right lobe, and the seminal vesicles were swollen. Under massage considerable reduction in size was apparent.

Treatment by massage of the prostate and the injection of 30 per cent. Argyrol into the deep urethra gave the patient considerable relief, but he remained under observation only a short time.

CASE IX.—*Attacks of abdominal pain of obscure origin caused by chronic prostatitis.* R. B., aged thirty-five years, farmer, married, seen October 12, 1911. Patient has never had any serious illness. Two or three years ago, in midwinter, when it was very cold, he was drawing logs and had an attack of what was called inflammation of the bladder. It was attended with a constant desire to urinate and some difficulty in passing urine, together with pain across the lower abdomen. In a day or two he was well again. About a year ago, while milking a cow, he was seized with severe pain in the right inguinal region. The pain was so intense that he could not get to his house. It lasted an hour and was followed by tenderness which persisted for a week. At times he has had a creeping and trembling sensation throughout the abdomen. Six days ago he began to have pain in the left side of the abdomen below the level of the umbilicus. The pain extended into the left testicle and lasted half an hour. Two days ago the pain recurred in the left groin, extending into the left testicle, and was associated with a cramping of the muscles on the inner side of the thigh. The pain was so severe that he was forced to lie down in the field. At no time was there difficulty in passing urine. At present he has so much tenderness that he is unable to work.

On examination a left-sided varicocele was found. The prostate was considerably enlarged and tender, the right lobe more than the left. The urine contained no blood. The patient was under treatment for only six weeks, but during that short time showed definite improvement, with no return of the painful seizures from which he had suffered.

CASE X.—*Attacks of pain in lower abdomen definitely relieved by treatment of prostate and deep urethra.* E. C., aged fifty-six years, farmer, married, seen January 6, 1910. Four years ago he began to have attacks of dull pain across the lower abdomen. If he became constipated the pain was likely to come on. At first the attacks were of a few hours' duration and occurred about once in six or eight weeks. Recurrence of pain has lately been more frequent. The seizures are usually associated with an increased desire to urinate, but he has no pain associated with urination. For the past three weeks he has been obliged to pass urine once during the night. Frequently the pain is relieved by movements

of the bowels. If he can have sexual intercourse when an attack appears to be impending he can usually avoid its occurrence.

The prostate and seminal vesicles were moderately enlarged and quite a little secretion appeared after massage. Catheterization showed half an ounce of residual urine in the bladder. Treatment consisted of massage and deep urethral instillations of 30 per cent. Argyrol. The patient showed steady improvement. During the early months of observation he was obliged to have fairly regular treatments in order to keep in good condition. If there was an interval of ten days between treatments he began to have an uneasy sensation about the prostate, perineum, and rectum, and if two weeks elapsed he was very certain to have a bad attack. Gradually he was able to take the treatments less and less often, until finally he could wait several months without suffering any evil results. The patient was seen last on June 27, 1914. He had not been treated for ten months, but stated that he had been very comfortable until within a few weeks. He had then experienced a recurrence of his old trouble, with severe pain in the lower abdomen, lasting two or three hours, and compelling him to lie down. The prostate was only a little enlarged, but was tender, hard, and nodular.

Case XI.—*Symptoms of general neurasthenia with no indications of disturbance of the prostate; chronic prostatitis discovered in course of routine examination.* T. L., aged thirty-five years, stenographer, single, seen September 30, 1913. Denies venereal infection. Has never been strong, but has had no serious illness. Patient has been nervous for about ten years. Complains of a full feeling in the ears and does not sleep well. Head gets tired after he works hard. He has a throbbing sensation in various parts of the body and the legs feel weak. Finds it hard to concentrate his mind. Is easily annoyed by trifles. Has frequent headaches and dizziness, and a cough which he considers of nervous origin. Urinates once or twice at night and rather frequently by day.

Examination revealed no organic anomaly save for the condition of the prostate. This was found to be moderately enlarged, soft, succulent, and very tender. After massage a profuse, purulent, yellow secretion literally poured from the penis. The patient has been under treatment for a year, and was last seen on August 15, 1914. The prostate was smaller but much firmer, and presented areas of softening alternating with small nodules. There was no special tenderness. The secretion expressed by massage was thinner and less abundant. The patient stated that his general health and nervous strength have been greatly benefited. He is able to endure more, can concentrate his mind more easily, sleeps better, and rarely has headaches or dizziness. The cough has disappeared.

These cases are illustrative of some of the common types of disturbance produced by chronic prostatitis. In many of them certain urinary or sexual symptoms might make one think of the

prostate as a possible source of trouble, but in others absolutely no indications are present to lead the diagnostician to the region of the pelvis. Young very aptly says that if the systematic and complete physical examination, so thoroughly emphasized today, were extended regularly to the prostate, many obscure conditions would be readily made clear. "The locality of symptoms is not of necessity the seat of disease" (McCrae), and the area to which the patient refers his complaints may be far from the primary source of trouble. It is well understood that pelvic disturbances in women may cause a great variety of reflex symptoms, often in distant parts, but it is not so commonly believed that similar conditions are encountered in disease of the male pelvic organs. Finally, a diagnosis of neurasthenia in the male is never justified unless a thorough examination of the prostate gland has been made.

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PRACTICAL OBSERVATIONS DRAWN FROM ONE HUNDRED AND SIXTY-ONE CASES OF HYSTERECTOMY.

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The subject of hysterectomy has been so thoroughly investigated that there seems to be little more left to be said as to its indications, its technique, or its results. Yet sometimes the retreading of the well-worn paths of experience may be productive of practical ideas and improved methods. We each develop our own ways of doing things, and we each may have experiences that are not common to all.

The development of this operation, which but a few years ago was considered one of grave danger and high mortality, to the point which has made it one of the safest procedures of abdominal surgery is a matter of history. Formerly the greatest dread of the surgeon was of infection or of hemorrhage, and many cases were lost from these complications. In the earlier operations each bloodvessel of the broad ligament was separately tied, making the operation tedious and difficult. Then the other extreme was reached in mass ligatures, which were productive of large necrotic stumps and insufficient care was taken in covering the raw places. It was not until we learned that ligatures applied to the six main trunks of the circulation adequately controlled all bleeding and made a safer operation with less danger of the ligatures slipping and less danger of morbidity from the raw areas left uncovered.

The technique of the modern operation for subtotal hysterectomy is simple, and simplicity should be the constant effort of all good surgery. When the average operation is well done it should leave a clean field and no raw surfaces. Panhysterectomy with its wide dissection often in a vascular and diseased field is by no means so easy of accomplishment.

A point somewhat neglected, but one which we have found to make the supravaginal amputation much easier, is that the appendages on both sides should be thoroughly freed of all adhesions and impediments, so that they are movable and can be brought up into the field before the clamps are applied or the broad ligaments divided. The writer recently observed a prominent surgeon doing a hysterectomy, start his dissection and removal beginning at the right side and working to the left in removing the uterus. When the mass had been removed a large part of a diseased ovary and tube was left on the left side still adherent to its bed, and the result was far from neat and satisfactory. If the appendage on that side had been thoroughly enucleated first, the removal would have been easy instead of difficult.

After everything is free, clamps are placed on the broad ligament. The infundibulo-pelvic ligaments on both sides are tied as well as the round ligaments. This is a necessary precaution, because if the clamp is depended on to hold them until the mass is removed, it is frequently found that they have slipped through the bite of the clamp, and that the vessel has retracted and is hard to find. The broad ligament is now divided on each side down to the uterus. The bladder is pushed down on front, revealing the course of the uterine artery. The artery is tied securely. Our custom is usually now to cut across the cervix carefully until the opposite side is reached, then to clamp the tissue containing the right uterine artery and with one stroke finish the amputation. The right uterine artery is now tied with a suture ligature. Three interrupted sutures close the cervical stump. The cervical stump is not usually disin-

fected in cases of simple fibromyomata, or unless there is an active acute infection present. In such case swabbing it out with iodin or iodin and carbolic acid seems to be all that is necessary. We have not had any bad results from this practice in the way of infections. As a rule the cervical canal need not be touched. A long running suture now carefully approximates the two layers of the broad ligament, starting at the right infundibulo-pelvic ligament, running down to the cervix, covering the cervical stump over with the reflected bladder peritoneum, and ending at the left infundibulo-pelvic ligament. Thus the field of operation is left as clean and as smooth as the face.

In view of the studies of recent years, showing that 60 to 80 per cent. of fibromyomata undergo some form of degeneration sooner or later, and are more or less associated with cardiovascular changes, whether they actually cause them or not, we are inclined to remove all palpable growths of any size, particularly if they are productive of symptoms. In the majority of cases they will eventually make trouble for the possessor of them.

Whenever it becomes necessary to extirpate both tubes and ovaries for any cause, conservative surgery would demand that the uterus be removed also. The only known function of this organ is that of an incubator for the fetus, a resting place where it may remain for nine months under proper conditions of temperature and nutrition. If there is no chance of its being used for this purpose, it only remains as a focus of infection, particularly if the appendages have been removed for pyogenic disease, or it may become the seat of carcinoma.

For the cases of simple fibromyomata without complications the mortality in competent hands should not be over 2 per cent. In those cases presenting pyogenic degenerations, severe complications from badly adherent pus tubes or cystic ovaries associated with extensive plastic exudate and infections the mortality is, of course, higher, the patients usually dying from peritonitis, septicemia, or shock in proportion to the difficulties and extensiveness of the complications that have to be attended to. The highest direct mortalities, as a matter of course, accompany the extensive Wertheim operations for carcinoma.

The difficulties of the operation are less frequently found in the large, movable fibromyomata. They are usually the easiest to remove. The easiest case perhaps in my series was that of a woman presenting an eighteen-pound tumor which could be rolled right out of the abdomen. Oftentimes the most difficulty is experienced with a rather small tumor located in a funnel pelvis, where the space for work is narrow and the tumor cannot be displaced upward. This is particularly so if the tumor is in the lower uterine segment posteriorly or under the bladder anteriorly or between the layers of the broad ligament. In one of the difficult cases met with by

the writer the tumor by pressure against the pubis divided the bladder into an upper and a lower chamber. Although the lower chamber was emptied by catheter before operation, the upper chamber was so distended that it could not be emptied so that the operation could proceed until the tumor mass was forced backward, allowing the urine to flow into the lower chamber and be catheterized.

The really difficult cases of hysterectomy are those in which one has to deal with extensive inflammatory affections of the appendages; cases in which there have been repeated attacks of pelvic peritonitis, leaving everything in the pelvis matted together with layer after layer of inflammatory exudate and associated with pus tubes, ovarian abscesses, or inflammatory cysts. The difficulties here are the difficulties of the complications involving adjacent organs, such as devitalized bowels from the separations of adhesions, injury to ureters or bladder, and the presence of large raw necrotic areas that have to be left because there is no way to cover them over. Ureters may have to be implanted, bowel may have to be repaired, resected, or covered over with omental grafts to avoid fecal fistulas, one of the most trying complications to be encountered. It is these cases that give the highest mortality outside of the carcinomata and present the greatest morbidity. They often suffer much pain afterward, but in many cases they ought to be thankful that they survive.

The following is a table of the indications for which hysterectomy was done in this series:

Simple fibroids	37
Submucous fibroids	4
Fibromatosis of the uterus	2
Fibroids and double pyosalpingitis	20
Fibroids and cystic ovaries	16
Fibroids, cystic ovaries, and pyosalpingitis	6
Double pyosalpingitis and infected uterus	38
Double pyosalpingitis and cystic ovaries	19
Infected uterus	3
Cesarian section with infected uterus	4
Carcinoma	11
Complete procidentia	1
Total	161

In the complicated cases those associated with many crops of old organized adhesions due to repeated attacks of pelvic peritonitis and the matting of everything together with plastic exudate it is the proper "clean up" after the operation *per se* that makes for the safety of the patient. Sometimes all anatomical relations seem to be lost in the mass of pathology, and the tangle must be carefully and patiently unravelled. If in doing so the bowel is denuded of its peritoneal layer the raw place must be turned in and stitched over. If this is impossible from the thickened and friable condition of things a piece of omentum may be grafted over the area, and in my

experience this has been found to be one of the most reliable methods of covering sometimes a hopeless area that would otherwise demand resection of the bowel. If the gut is too badly involved then indeed resection is at times necessary. Failure to take care of these details in a painstaking way and to look out for every raw and injured area may result in a fecal fistula, an ileus, or some other trying and at times fatal complication. Nowhere in the human body is it more necessary to make every detail of the operative technique perfect than in the abdominal cavity, for when once the work is finished and sewed up there is no way to take a daily look at what is going on, as might be done with an amputation or other external operation. The careless placing of a suture that might leave a fecal leak, or the omission to cover over a weakened place in the gut, or the slighting of what may sometimes seem a trivial detail, may destroy the work of an otherwise brilliant operation and cost the patient her life, and this is true of all abdominal surgery.

CEREBRAL EDEMA (WET BRAIN) IN CHRONIC ALCOHOLISM.

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Our paper concerns itself with a phase of chronic alcoholism, to which the pathologically prominent change has given the name cerebral edema, or wet brain.

The clinical complex, which we purpose elaborating has been given scant place in the literature upon complications of alcoholism; only the most cursory mention of it, in fact, is made in any publication, with exception of two American texts. Dana[1] seems to have been the first to recognize the condition. His description is very complete in most details, and it is only because of our considerable experience with wet brain at the House of Correction Hospital, Chicago, and because we presume to add to the picture both from the point of view of clinical manifestations and differential diagnosis, that we reopen the subject.

Lambert[2] is the other American who describes cerebral edema

[1] Text-book of Nervous Diseases and Psychiatry, 7th edition, p. 444 et seq.
[2] Modern Medicine (Osler), I, p. 186, et seq.

at some length. He, too, lays stress upon the meagerness of literature relative to the subject, and credits Dana with the first recognition of this phase of alcoholism. Standard works, such as Oppenheim,[3] Lewandowsky,[4] and Curschmann,[5] speak only of a serous meningitis which may be traced, in some cases, to chronic alcoholism. This type of meningitis, however, we would emphasize at the outset, is something quite distinct from the condition which is the topic of our paper. It is true that long-continued alcoholic overindulgence may be associated with serous meningitis; the latter, however, may be secondary to a number of factors, toxic, infectious, traumatic, and mechanical, and presents clinical features indicative of gross nervous changes, such as pareses, pathological cerebrospinal fluid and the like. Alcoholic cerebral edema, on the other hand, is, to all appearances, a toxic vascular phenomenon, and its correlated clinical manifestations are not similar to those of inflammations of the brain or its coverings.

Wassermeyer,[6] in his exhaustive monograph on delirium tremens, gives no place to the train of symptoms which we look upon as characteristic of wet brain and the general absence of reference to the subject in foreign literature, brings up the question whether we may not see alcoholics under conditions differing from those generally obtainable elsewhere. About 2500 cases of alcoholism come under our observation annually. They include patients of every age, sex, and social condition; as to the last, however, the great majority are from the lowest stratum of society. Some have been subjected to trauma of one kind or another; others are suffering from an infection, acute or chronic. Most of the patients are naturally enough accustomed to the cheapest alcoholic beverages. All of these factors are present in practically equal degree in most American public hospitals, and, so far as our personal knowledge goes, in German and Austrian institutions, too, so that we feel justified in assuming that we are working under no unusual conditions.

Wet brain, dissected out from the network of alcoholic complications and sequelæ regularly associated with it, is definitely delimited in nearly every respect, particularly as to classification, symptomatology, and prognosis.

Our view as to its place in the phase of chronic alcoholism has undergone change from time to time. Certain etiological factors deserve emphasis: (1) the longer the history of alcoholism and the more frequent the attacks of delirium tremens the more likely is the patient to develop wet brain, and one attack predisposes to a second; (2) some patients regularly go over into the wet-brain state from each attack of delirium; (3) cerebral edema always

[3] Lehrbuch der Nervenkrankheiten, Berlin, 1908, II, S. 1087.
[4] Handbuch der Neurologie, Berlin, 1911, II, S. 1903.
[5] Lehrbuch der Nervenkrankheiten, Berlin, 1909, S. 524.
[6] Archiv. f. Psychiatrie und Nervenkrankheiten, 1908, xliv, S. 861 et seq.

follows, never precedes, delirium tremens; (4) an unambiguous instance has never come under our observation of edema occurring independently of an immediately preceeding delirium, though Dana mentions the possibility of such an occurrence.

The close relationship to delirium tremens is evident, but whether wet brain is a sequela of *mania a potu*, an equivalent of the same, or an independent phase of chronic alcoholism has not been an easy problem to solve. We are strongly of the opinion, however, that delirium tremens in its classic form and wet brain represent merely successive time events in the alcoholic cycle, and that the pathological condition, wet brain, might aptly be called, clinically, comatose delirium tremens.

A long period—seven to ten years—of overindulgence in alcohol precedes the onset of the condition. This is the incubation period of delirium tremens. For some reason, as yet quite unknown, the individual develops delirium. Hypotheses are not wanting, however, to explain the transition. Among other causes suggested have been auto-intoxication, that first-aid explanation in so many doubtful conditions. According to the views of E. Meyer,[7] Ganser,[8] Ziehen,[9] and others the long alcoholic abuse renders the gastro-intestinal tract and liver incapable of destroying toxins or renders them susceptible to pathogenic organisms, with the result that the poisons accumulate and at a given time overwhelm the individual. The same view is held by some to explain the origin of liver cirrhosis in alcoholics, a theory supported by experimental work.

The hypothesis of Wagner V. Jauregg[10] is an ingenious one. It, too, is based on a toxic theory, namely, alcohol gives rise to a toxin and an antitoxin which neutralize each other as long as alcohol is exhibited. When the drug is withdrawn the antitoxin is no longer formed, with a consequent preponderance of the poison. This view is surely untenable, however, as many of our patients developed delirium after a prolonged spree, not after withdrawal of the alcohol. Starvation with its sequelæ, as seen in other conditions, is also advanced as an explanation, and has much in its favor, for it is well known that the alcoholic can take practically no food while he is drinking and, further, that the taking of nourishment goes hand in hand with improvement.

We shall not tarry longer on this interesting topic, as it does not concern itself immediately with the wet-brain condition. The predisposing factors of delirium tremens—pneumonia, trauma, especially fractures of the long bones, mental shock, combined with with a period of excessive alcoholism or a sudden withdrawal of the drug, these are all too well known to be dwelt upon.

[7] Ursachen der Geisteskrankheiten, Jena, 1907, S. 138.

[8] Zur Behandlung des Delirium Tremens, Münch. med. Woch., 1907, No. 3., S. 122.

[9] Psychiatrie, Leipzig, 1902, 2 Aufl.

[10] Quoted by Wassermeyer, q.v.

Delirium tremens shows itself in several forms. In the undeveloped type, or *forme fruste*, the so-called "touch of the horrors," the patient exhibits a vague uneasiness, starts at slight noises, may have ill-formed hallucinations of sight and hearing, is restless, loses sleep, has disturbed dreams, paresthesias, marked tremor of the hands and tongue, and a constant fear that some evil will overtake him.

The incipient period has a variable duration, usually two to three days, yielding to appropriate therapy—a good hypnotic, followed by sleep—or going over into the fully developed delirium tremens. The latter with its well-known features we shall not dwell upon except to bring to your attention a further subdivision into types which we observe with unequal frequency. These types are more or less comparable in their manifestations to the two ways in which excessive heat affects men, namely, heat exhaustion and thermic fever. In the first form, occurring in about one-fourth of all, and showing the highest mortality, there is profound asthenia, pallor, cold skin, a rolling of the eyes from side to side, and often subnormal temperature; whereas in the more frequent second type there is observed a flushed face, a full-bounding pulse, great mental and motor excitement, and possibly fever. The former requires heat and analeptica, the second cold packs and sedatives; both demand strychnin to replace the alcohol. The deciding factor as to which of these sub-types of delirium will occur is possibly the previous integrity of the cardiovascular system.

Delirium tremens, when treated, ordinarily lasts three to eight days, perhaps oftenest five, though some cases tend to continue, with clear intervals, for several weeks. In about 10 to 15 per cent., however, there is an entirely different outcome and the condition called wet brain or, better, comatose delirium tremens supervenes.

The transition from delirium to edema is fairly well marked. Striking is the semicoma succeeding the active delirium. The latter is now of a low muttering type, the individual lies with his eyes closed and is aroused with difficulty. Supraorbital pressure and rubbing of the knuckles briskly over the chest in the mid-axillary line bring about a momentary lifting of the stupor, but questions will not elicit intelligent answers. During the early stages he will swallow food and still retain consciousness enough to have delusions and hallucinations resembling a low typhoid delirium. The pulse is rapid and weak; the temperature elevated a degree or more. Conjunctivitis is common, the tongue and teeth are sordes-covered, the breath is foul, and albumin is usually present in the urine.

The train of symptoms peculiarly indicative of wet brain are essentially those of meningeal irritation and of cerebral compression. Hyperesthesia is one of the most marked and constant features; the integument is ultrasensitive, and pressure on the muscles causes

the patient to grimace and moan and try to draw himself away. Photophobia, however, is absent; as the individual does not complain we can form no judgment as to the presence of headache. Vomiting is not observed.

Rigidity in its various manifestations is always prominent, occupying with hyperesthesia the centre of the wet-brain picture. The degree to which it is present is significant of the severity of the particular case; thus Dana remarks that when the neck becomes stiff the outlook is hopeless. Kernig's sign is always present to some extent; toward the end it becomes marked.

The deep reflexes are early increased, as is the rule in delirium tremens; later, with the increase in the edema, they are lost. The pupils are usually small, equal, regular, responding sluggishly to light; they dilate somewhat if the patient can be aroused, narrowing down once more as he relapses into coma. In a small percentage of cases we have observed one or all of the criteria of the Argyll-Robertson phenomenon—usually the reflex rigidity—a condition which other observers, notably Nonne,[11] Uhthoff[12] have described in long-standing alcoholism. It is a mooted question whether this pupillary condition is permanent or not.

We are not yet prepared to express ourselves definitively as to the cerebrospinal fluid in wet brain. Cytoanalysis gives normal results; globulin and Wassermann reactions, in frank cases, are negative. It is in regard to the pressure under which the fluid exists that we withhold our opinion. Dana in his cases seems to have found a high tension the rule. He does not state, however, the means he employed to determine the pressure. As will be brought out later, there was no indication at autopsy in our cases that the cerebrospinal fluid *intravitam* was under increased tension. Clinically we have made no manometric obervations, judging the pressure only by the velocity of flow accurate enough, perhaps, in a relative way. The fluid does not spurt out, as in meningitis, for example, but comes out drop by drop, with a rapidity not much different from normal. The many pathological changes recorded as characteristic of the fluid in the hybrid serous meningitis are regularly absent. In brief if the fluid is not free from abnormalities an uncomplicated case of wet brain is not present.

Side by side with the meningeal picture, except in very rare instances, to which we shall refer below, is another, not an integral part of the wet brain, but pointing rather to one of the infectious complications so regularly accompanying alcoholism. The commonest of these by far is pneumonia, usually patchy in character,

[11] Klinische und anatomische Untersuchung eines Falles von isolierter echter reflectorischer Pupillenstarre Ohne Syphilis, bei alcohol chron. gravis-Neurolog, Zentralblatt, 1912, xxxi, 60.

[12] Graefe-Saemisch-Handbuch der Augenheilkunde, Leipzig, 1901, 2 auf. Band xi, abt. 2a. S. 24.

and accounting for the temperature, tachycardia, tachypnea, leukocytosis and the like. This associated infection clouds the wet-brain picture and demands extreme caution in making a diagnosis. Neither Dana nor Lambert has dwelt at any length upon this interweaving of conditions, and it has taken us several years to feel assured that there is a meningeal phase of delirium tremens, and that it is not a manifestation of the co-existing infection.

In six instances no gross pathological lesion was found to account for the symptoms of some infection in the wet-brain complex. It has occurred to us that these may be examples of what Magnan[13] has called delirium tremens febrile. The possibility, however, of a microscopic bronchopneumonia or of some unrecognized septic condition must be admitted. Temperature and other signs of infection are hardly compatible with an uncomplicated wet brain.

All of our deaths are made "coroners' cases." Since July, 1911, in practically all instances, Dr. E. R. Le Count has performed the postmortem examinations, and to him we are indebted for the following:[14]

"As a rule, edema of the brain in delirium tremens is characterized by two features, which, although they do not serve to distinguish it invariably as to etiology, are, nevertheless frequently helpful in determining the cause of death; for without knowledge of the clinical conditon, it may be difficult to conclude from any postmortem examination that death was due to delirium tremens.

"The pia-arachnoid membranes are lifted away from the brain over the vertex, both in front and behind, but principally anterior to a line passing over the head between the external auditory meati. The fluid, as it is seen under these transparent membranes, appears slightly yellowish. In a glass pipette it is quite c[illegible] and colorless; naturally the fluid is most abundant opposite the sulci, but in many instances it is so plentiful that the arachnoid, or the outermost portion of the pia-arachnoid is lifted away from the surface or highest part of the convolutions.

"The fluid is, strictly speaking, in the loose meshwork which connects the arachnoid with the pia, for when the outer layer is broken or torn away and the fluid released there still remains the vessel-bearing part of the pia covering the brain.

"The other feature is more noticeable after the brain is removed. It is a widening of the sulci and a narrowing of the convolutions, principally of the frontal and parietal lobes. This may be general for these regions, but often there are places where pits with dimensions of 2 to 3 cm. and 0.5 cm. in depth occur—pits into which

[13] Alzheimer, Das Delirium alcoholicum febrile Magnan. Centralblatt f. Nervenheilkunde und Pschyiatrie, 1904, S. 437.

[14] Personal communication.

about one-half of the terminal phalanx of the little finger may be laid. These pits, or more marked and localized regions of atrophy, are at the meeting-points of the sulci.

"There is a more or less prevalent idea in medical literature and circles that a fibrous lepto-meningitis in patches, may result from the long-continued use of alcoholic beverages. I have not found it with any regularity in the brains of persons dying of delirium tremens, and it certainly is not as characteristic as the two features emphasized.

"Another change is a softening or increased moisture of the brain tissue; but this, too, is inconstant and in some measure probably connected with cadaveric decomposition. In some instances the finer arterioles of the pia are more engorged with blood than in others; this apparently is associated with a type of active or maniacal delirium rather than with those showing a lethargic or semicomatose delirium. The atrophy of the cerebral cortex and the accumulation of fluid have impressed me as an edema *ex vacuo;* and, certainly, there is no indication at the postmortem examination that the fluid during life is under an increased pressure."

Wassermeyer nowhere makes mention of a cerebral edema similar to the above. Dana, on the other hand, who has autopsied twenty of his own cases of wet brain, found such a condition, and from it coined the name. It is most marked, according to him, in the arachnoid and subarachnoid spaces, and may penetrate into the brain substance for a variable distance. An increase in the ventricular fluid content is also not infrequent, with consequent dilatation of the ventricular spaces. As for the remainder, Dana's findings are not different from those of delirium tremens. The picture of the latter, we digress to say, is by no means a constant one, as Wassermeyer points out. He emphasizes the hyperemia, the frequent capillary, less often extensive, hemorrhages; the occasional thickening of the meninges; and in some instances the presence of a condition indistinguishable from the poliomyelitis acuta hemorrhagica superior of Wernicke and in others from a pachymeningitis hemorrhagica interna. Finally there may or may not be evidence of degeneration in the nerve cells or a growth of the glial tissue.

It would seem, therefore, that the more or less extensive fluid accumulation in the arachnoid, with the widening of the sulci and the narrowing of the convolutions, constitute the salient autopsy findings of wet brain. As there is no evidence of the fluid's having existed under increased pressure, it might be urged that the primary change is cerebral atrophy and that the fluid is secondary, much like the *vacatwucherung* about the kidneys when the latter atrophy and the space they formerly occupied is filled with a compensatory fatty deposit.

The diagnosis of alcoholic cerebral edema may be extremely

easy or, on the other hand, impossible. When there has been opportunity to observe the patient through the phases of incipient and fully developed delirium tremens there is, as a rule, no difficulty; the same is to a great extent true in cases which are brought into the hospital already suffering from frank delirium tremens, especially when there is no history of trauma. At times the comatose form of delirium tremens may have to be distinguished from the ordinary form (especially from the sub-type we have called asthenic); the semicoma in the former, the hyperesthesia and rigidity, the absence of the rolling of the eyes, etc., usually serve to differentiate the two; in addition following wet brain there is usually a total amnesia, while after delirium tremens the individual commonly recognizes part of his hallucinations, as such, or he may jumble halluncinations and facts.

A history of, or the possibility of, trauma may cloud the diagnosis almost beyond the possibility of solution. With us basal skull fracture is the condition above all others to be kept in mind, as bitter experience has shown time and again. The following points have been of the greatest value in the diagnosis of basal fractures, in the absence of cerebrospinal fluid or blood from the ear or nose; delayed ecchymoses over the mastoid and about the orbit; eye-muscle palsies; paretic involvement of one or more extremities; and blood in the spinal fluid.

A number of other conditions must likewise be taken into account. The meningitides can, usually, be ruled out by the negative bacteriological, serological, and chemical cerebrospinal fluid tests, according to the type present. Uremic coma, which may present great difficulties both because of a marked similarity to wet brain on the clinical side and also because most alcoholics show renal changes, is recognized by the associated cardiovascular phenomena, retinal changes, by the exaggerated knee-jerks usually present, the absence of hyperesthesia, and the occurrence of convulsions and vomiting. Cerebrospinal lues is distinguished by the Wassermann and globulin reactions, by cyto-analysis in the spinal fluid, and by the presence of definite organic changes in the nervous system Cerebral hemorrhage, thrombosis, and embolism are suggested by etiology and by the organic nervous findings. Finally, pachymeningitis, hemorrhagica interna, and polioencephalitis acuta superior of Wernicke must be thought of because of the common etiology—alcohol. In these, however, gross nervous changes are distinguishing characteristics.

The duration of wet brain is variable, the condition lasting from two to twelve weeks, usually about three. The mortality is nearly 75 per cent.; death may occur at any time, oftenest from a bronchopneumonia, which frequently can scarcely be diagnosed in view of the paucity of physical signs. Unfavorable symptoms, indicative of an increase in the edema, are augmented muscular rigidity

especially of the neckmuscles, diminution in the size of the pupils and more marked sluggishness in their response to light, and deepening of the coma. The pulse finally becomes rapid and feeble, there is incontinence of urine and feces, and death occurs.

As to treatment, aside from symptomatic measures, little can be done. The death rate would indicate this. Cardiac stimulants are in order. The nutrition of the patient suffers markedly consequent upon the long state of coma; persistent effort should be made to force liquids; and in the severer cases it may be necessary to give alimentation by the nasal tube. Elimination must also not be neglected. Ergot we have found harmful as compared with its usefulness in the asthenic type of delirium tremens. Lumbar puncture has been of no service in our hands, contrary to favorable reports by Dana. Scientific hydrotherapy, now not available to us may prove an important addition to our therapeutics.

Resumé. After long-continued overindulgence in alcohol an individual, for reasons as yet undetermined, develops delirium tremens. The latter usually manifests itself in three stages: incipient, fully developed (classic), and comatose (wet brain). The symptoms of wet brain are essentially meningeal, semicoma, generalized hyperesthesia, and muscular rigidity (Kernig and neck rigidity) standing out prominently; the more marked are the latter two features, the graver the prognosis. The cerebrospinal fluid is, to all appearances, normal. The mortality is nearly 75 per cent. Necropsy reveals no gross lesions aside from the more or less marked fluid accumulation in the pia-arachnoid space, a widening of the sulci, and a narrowing of the convolutions to account for the symptoms of changes in the brain. Associated with the cerebral edema complex there is very often bronchopneumonia, which clouds the diagnosis and usually is responsible for death. The differential diagnosis must concern itself particularly with the possibility of a concomitant skull fracture which may easily be obscured by the nervous manifestations of comatose delirium tremens.

THE STUDY OF TWO HUNDRED AND FIFTY STAINED BLOOD-FILMS IN PYORRHEA ALVEOLARIS.

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The object of this paper is not to discuss the etiology or the prognostic value of the stained blood-film. It is written for the purpose of informing the reader that tinctorial changes and an increase of the large lymphocytes are common findings in the stained blood-films made from patients affected with pyorrhea alveolaris.

Six years ago, by chance, a stained blood-film from a patient affected with pyorrhea alveolaris was examined microscopically. The picture which this stained blood-film presented was a very interesting one. On close observation it showed a wide variation tinctorially of the stained leukocytes. Thinking that a mistake had been made in the technique of preparing and staining the blood-film, a second blood-film was made. The technique employed to prepare and stain the second blood-film was the same as had been used to prepare and stain the first blood-film. Microscopically the second blood-film showed that the stained leukocytes were tinctorially and in number a duplicate of the first stained blood-film examined.

Having observed the tinctorial changes of the stained leukocytes, the next step was to determine if the differential blood-count of the stained films showed the normal proportion of the different varieties of leukocytes. The differential count when finished presented an interesting picture. The large lymphocytes and the irritation forms of Ehrlich were increased in number, while coincident with this change the polymorphonuclear neutrophiles were diminished in number, as were also the small lymphocytes. At the time of this observation the author was busily occupied in the study of the growth rate of some of the pathogenic bacteria of the mouth associated with pyorrhea alveolaris, and as a result thereof further study was deferred.

Two and a half years ago the author commenced to make it a matter of regular routine to make a blood-film from all patients consulting him relative to pyorrhea alveolaris, and also from all patients treated for pyorrhea alveolaris. The findings of the differential blood-count of each case were recorded with the other clinical findings.

To avoid the possibility of error in the staining of the blood-films the following precaution was taken: Wright's blood-stain was made as described by its originator. After being made it was allowed to dry thoroughly, then it was dissolved in methyl-alcohol made by C. A. F. Kahlbaum. The reason this alcohol was used was because it was neutral when titrated. By observing the above step one can, we believe with safety, exclude the possibility of error which might have entered if different batches of Wright's stain had been used.

The interesting features of the stained blood-films are: the wide variation of the stained nuclei and cytoplasm of the leukocytes; the morphological changes of the nuclei and cytoplasm; the increase of the large lymphocytes and the irritation forms of Ehrlich; with the coincident decrease of the polymorphonuclear neutrophiles, and small lymphocytes. The following summary shows the variation in the number of the different varieties of leukocytes: polymorphonuclear neutrophiles, 45 per cent. to 60 per cent.; large lymphocytes, 15 per cent. to 30 per cent.; small lymphocytes,

5 per cent. to 15 per cent.; eosinophiles, 1 per cent. to 3 per cent.; mast cells, 1 per cent. to 2 per cent.; transitionals, 1 per cent. to 3 per cent.; irritation forms of Ehrlich 3 per cent. to 10 per cent.; degenerates, variable in number.

At a glance one notes that on comparing the above figures of the differential count of the blood-film of a patient affected with pyorrhea alveolaris to the normal number of the different varieties of leukocytes that the large lymphocytes and the irritation forms of Ehrlich are in excess and that the polymorphonuclear neutrophiles and the small lymphocytes are diminished in number. The excess of the large lymphocytes, which together with the small lymphocytes brings the total number of the lymphocytes far above the number of these cells contained in the normal blood, in the condition presented, is known hematogically as lymphocytosis.

Returning to the study of the stained blood-films and beginning with the large lymphocytes, there is noted a wide variation of the intensity and shade of the stained nuclei. They vary tinctorially from an intense reddish-violet to a pale reddish-violet or from an intense blue to a very pale blue. Sometimes there appears in the same field a variably stained reddish-violet nucleus and a variably stained blue nucleus. Other specimens present a nucleus which is faintly stained, and at times it is scarcely descernible.

Contained in the substance of the nucleus of the large lymphocytes there are present granules which are variable in size and in shape, and have no definite arrangement. In some of the nuclei of the large lymphocytes they are reduced to a dust-like fineness. As a rule the granules of the large lymphocytes are stained the same, but a slightly darker color than the nuclus. When the granules are reduced to a dust-like fineness they are stained a dirty shade of reddish-violet or blue. In some specimens the nuclei may be well stained and the granules are poorly stained, while in other specimens the nucleus is poorly stained and the granules are distinctly stained.

The cytoplasm surrounding the nucleus of the large lymphocytes is also subject to a wide variation tinctorially. The cytoplasm of one large lymphocyte may be stained a reddish-violet, while that of another one in the same field is stained a pale blue. Or it is stained a quite intense reddish-violet, and that which surrounds the nucleus of an adjacent large lymphocyte is stained a delicate reddish-violet. Or that which surrounds the nucleus of another large lymphocyte is stained a sharp, well-defined blue, and that which surrounds the nucleus of another leukocyte, this variety is stained a pale blue. Occasionally the nucleus of a large lymphocyte is stained a beautiful shade of reddish-violet and the cytoplasm surrounding it is stained an excellent shade of blue, which stands out in bold contrast to the color of the nucleus.

Morphologically the large lymphocytes vary in size and in shape. The nucleus may be located centrally or excentrically in the cyto-

plasm. The nucleus varies from a round to a semilunar shape; its margins are, as a rule, smooth and regular in outline, but occasionally they are quite rough and irregular in outline. The margin of the cytoplasm surrounding the nucleus is, as a rule, smooth and regular in outline, but occasionally it is irregular and rough in outline. The cytoplasm of this variety of leukocyte varies from round or square to a semilunar shape.

The nuclei of the polymorphonuclear neutrophiles, like the nucleus of the large lymphocytes, are variably stained. Some of them are stained a reddish-violet, which varies in intensity from a dark shade to a light shade of this color. The nuclei of other specimens of this variety of leukocyte are stained blue, which varies in intensity from a dark shade to a light shade of this color. In some of the blood-films there appear in the same field a nucleus which is stained a variable reddish violet and the nucleus of another leukocyte of this variety which is stained a variable blue. Many times one notes that the nuclei of the polymorphonuclear neutrophiles are found free from any cytoplasm. These nuclei are stained a variable reddish-violet or blue. They should not be classed as degenerates, but should be tabulated with the other polymorphonuclear neutrophiles. The absence of the cytoplasm does not necessarily indicate that it is not present, for in all likelihood it is, and its apparent absence is the result of some chemical reaction which prevents it from taking the stain.

Contained in the substance of the nuclei of the polymorphonuclear neutrophiles are granules which are variable in size and in shape, and which are scattered without any definite arrangement in it. Sometimes the granules are reduced to a dust-like fineness. As a rule they are stained several shades darker of the same color as the nucleus. When the granules are reduced to a dust-like fineness they are stained a dirty reddish-violet or blue of varying intensity.

The cytoplasm of the polymorphonuclear neutrophiles like the nuclei has a wide variation of color. The cytoplasm surrounding one nucleus is stained a dark reddish-violet, while that which surrounds the nucleus of a neighboring cell is a light shade of this color, or it is stained a variable blue, or it may be stained a blue which has a reddish tinge, or it may be stained a delicate pinkish red. Any of the colors may be the predominating color of a stained blood-film, or, as is sometimes observed, any two or them or all of them may be noted.

Contained in the cytoplasm of the polymorphonuclear neutrophiles are round granules which vary in size from dust-like fineness to round bodies about the size of a small pinhead. The granules are variably stained, some of them are a reddish blue, others a reddish-violet; others are a dirty pale blue, while others tinctorially vary from a pale pinkish-red to a sharp red.

The irritation forms of Ehrlich found in the blood-film of a patient

affected with pyorrhea alveolaris are, as a rule, distinctly stained a reddish-violet or blue, the variation tinctorially of this variety of leukocyte being very slight.

The shape of this variety of leukocyte is variable: some of them are uniformly elongated, others are irregularly elongated, one extremity being much larger than the opposite one, or they may be somewhat round in shape. The margins of the stained nucleus may be irregular and smooth in outline, while others are irregular and rough in outline. In some of the nuclei of this variety of leukocyte, granules are noted which are irregular in size and in shape and have no definite arrangement. The granules are, as a rule, stained darker than the nucleus, but are of the same color which it is stained. In other leukocytes of this variety there are found in its substance vacuolated spaces which when present are variable in size and in shape and have no regular arrangement. At present the stains which are used to stain blood-films do not demonstrate a cytoplasm surrounding the nucleus of this variety of leukocyte.

The small lymphocytes observed in the stained blood-films from patients affected with pyorrhea alveolaris are more constant tinctorially. The color which they are stained is a rich reddish-violet or sharp, well-defined blue.

Contained in the nucleus of the small lymphocytes are granules which are variable in size and in shape and have no definite arrangement. They are stained several shades darker than the nucleus, but are of the same color that it is stained.

The cytoplasm which surrounds the nucleus of the small lymphocyte is scant in amount when compared to the quantity which surrounds the large lymphocyte, in some instances it being so very small in amount that it is quite difficult to find it. The stained cytoplasm of this variety of leukocyte is quite uniformly a deep reddish-violet or deep blue.

The small lymphocyte morphologically is quite uniform, showing little if any deviation from the normal.

The degenerated polymorphonuclear neutrophiles also present a very interesting picture. The nuclei of the degenerated cell are widely separated when compared to their normal position in the cytoplasm when the cell is intact. The granules likewise are scattered over a considerable area. The position of the nuclei and the granules of the degenerated cell suggest an explosion of it. The nuclei of the degenerated cell are variably stained; some of them are reddish-violet or varying intensity, others are stained various shades of blue, while the nuclei of others are scarcely stained at all. The granules are stained many shades of reddish-violet, blue, and red.

From the foregoing description of the many varieties of the tinctorial changes and the changed proportion of the different varieties of leukocytes observed in the studied blood-films it may well be

asked what practical significance has all this? The answer is that the study of the stained blood-films in this paper emphasizes the importance of a better understanding of the blood changes and their significance which occur in the blood of patients affected with one of the greatest plagues with which the body of civilized man is at the present cursed, pyorrhea alveolaris.

Many diseases are at the present time identified by the changes observed in the differential blood-count, namely, chlorosis, pernicious anemia, myeloid leukemia, acute and chronic leukemia, etc. One cannot overlook with discretion the possibility that the changes observed in the differential blood-count in pyorrhea alveolaris may be of value.

No doubt much will be done in the future to interpret the meaning of the changes in the staining properties of the leukocytes and the relative changes in number of the different varieties of leukocytes observed in the differential blood-count of patients affected with pyorrhea alveolaris. The findings perhaps will be interpreted etiologically and also prognostically; perhaps not by the dentist, but by his colleague the trained medical man. One cannot at the present forecast what tomorrow or a year from now may have in store for the investigator as to the relation of the change in staining and the lymphocytosis observed in pyorrhea alveolaris. These changes may be the key which will open the long-locked chest in which is hidden one of the causes of pyorrhea alveolaris.

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REVIEWS

A Text-book of the Practice of Medicine for Students and Practitioners. By Hobart Amory Hare, B.Sc., M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital. Third edition, revised and enlarged. Pp. 969; 142 illustrations and 16 plates in color. Philadelphia and New York: Lea & Febiger, 1915.

The appearance of the third edition of Dr. Hare's text-book of medicine will be received with pleasure by those who have studied the former editions of this volume and those who have become acquainted with the other text-books of the distinguished author. The wide popularity of Dr. Hare's other publications demonstrates the worth of the matter that comes from his pen, and this present book presents no exception to the character of his previous work. The book is written in a remarkably clear, smoothly-expressed style, so that he who reads, acquires knowledge of medicine and enjoys at the same time the ease and grace with which the subject is put forth.

The contents follow the following order: first the infectious diseases are discussed, then the diseases of the several systems and organs of the body, the intoxications, the disorders of the nervous system, and finally the functional nervous diseases and diseases of disputed pathology. Each disease is discussed under the sub-heads of definition, etiology, morbid anatomy, symptoms, prognosis, and treatment. Of these sub-heads in general it is found that the sections dealing with symptomatology and treatment are splendid, as would be expected; the sections upon etiology are fairly complete, but greater interest would be added to them by a more complete exposition of the pathogenesis and mode of action of the various diseases; and the section upon pathology would be benefited by the addition of comments upon the pathological-physiology of the disorder under discussion.

Here and there throughout the book are found, occasionally, a few points which seem open to criticism. It hardly seems necessary to include various laboratory procedures in a book of this type; epidemic sore throat might be classified properly in the infectious diseases; pellagra, though still a subject of dispute, with beri-beri;

the several arrhythmias could be more completely discussed and several types that are omitted should be included; no mention is made of vagotonia and sympathicotonia; only the phenolphthalein test of kidney function is mentioned, and no reference is made to its application in the various nephropathies; the statements regarding the wiring of aneurysms are, most properly, quite conservative; lastly, it may be questioned if women of a "lean, lank type" should be compared to a "hunting dog in training."

J. H. M., Jr.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics, Materia Medica and Diagnosis in the Jefferson Medical College; Physician to the Jefferson Hospital, etc. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. III, September, 1914. Pp. 339; 41 illustrations. Vol. IV, December, 1914. Pp. 413; 102 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

CONTINUED experience with this quarterly has convinced us that for a work of its kind it is unequalled in English. The contributors are all men of distinction in their respective fields, their articles are invariably carefully compiled, and their comments and criticisms are always illuminating and helpful.

In Vol. III, William Ewart discusses diseases of the thorax and its viscera, paying particular attention to tuberculosis, physical examination of the chest, and the organs of circulation. Dermatology and syphilis are taken up by William S. Gottheil, who particularly emphasizes the new serum treatment in dermatology. Obstetrics is covered by Edward P. Davis, who includes obstetric surgery and conditions of the newborn in his complete review of the entire subject. A really excellent article on diseases of the nervous system, by William G. Spiller, concludes the volume.

The last volume for 1914 opens with a long contribution by Edward H. Goodman on diseases of the entire digestive tract. John Rose Bradford follows this with a few pages on diseases of the kidneys, whereas genito-urinary diseases are taken up at length by Charles W. Bonney. One of the most interesting contributions is that by Joseph C. Bloodgood, who takes up a wide range of important subjects, namely: The surgery of the extremities, shock, anesthesia, general and local infections, fractures and dislocations, and tumors. As usual, one of the most practical contributions for the entire year is H. R. M. Landis' therapeutic referendum, in

which he discusses critically many of the most important questions of modern therapeutics.

We cannot refrain from reiterating an opinion already expressed in these reviews, that whoever desires to be well informed about the advances that are continually taking place in the medical sciences, cannot do better than to become well acquainted with the admirable contributions for which *Progressive Medicine* is conspicuous. G. M. P.

THE COMMONER DISEASES: THEIR CAUSES AND EFFECTS. By DR. LEONHARD JORES, Professor of Pathology and Pathological Anatomy, University of Marburg. Authorized English Translation by WILLIAM H. WOGLOM, M.D., Assistant Professor in Columbia University, Assigned to Cancer Research. Pp. 424; 250 figures in the text. Philadelphia and London: J. B. Lippincott Company, 1915.

THE presentation of a familiar subject in a new form is always interesting and often valuable because it gives a new point of view to the reader and tends to impress him by its very novelty. It is this element which gives particular value to the collection of a series of articles upon special pathology by Dr. Jores, which were just presented as lectures to his students at Marburg. Each article deals primarily with gross pathology, omitting entirely questions of morphology or of differential diagnosis and showing in what way anatomical changes can produce physiological upsets and complications. It is the newer conception of disease, which has spread so rapidly in the past few years, that the clinical manifestation of any disorder are due almost entirely to disturbances of function of the diseased organ, or organs in close relation to the diseased one. Jores assumes this to be true, but throughout his work endeavors to show that pathological changes are the real basis of disease, while at the same time demonstrating the functional derangements that are produced by the morbid processes. This method of presentation of pathology, considering it largely from the viewpoint of disturbed physiology is a novel one and one that can not help being interesting to those accustomed to the long description of morphological changes and minute anatomy that are found in the usual text-book of pathology.

To consider the book more in detail, it may be said that the various chapters follow no consecutive order but skip from subject to subject and by no means include descriptions of all disorders that may occur. The discussion of etiology and pathogenesis is particularly good, so that in many cases one wishes that it might be even fuller and more complete and detailed than it is. The illustrations are

superb and are really valuable in showing and emphasizing what the author wishes to teach. The references are quite complete, but very graphically illustrate the present-day attitude of the German mind. There are hundreds of references to German works, but the work of investigators in other countries is almost completely ignored. Their work, not having been done in Germany, is of course, not comparable to that which has been produced by the Germans. J. H. M., Jr.

OPERATIVE SURGERY: THE HEAD AND NECK, THE THORAX AND ABDOMEN. By EDWARD H. TAYLOR, Professor of Surgery in the University of Dublin. Pp. 505; 300 figures from original drawings, many printed in colors. New York: William Wood & Co., 1914.

THE author confines himself almost entirely to the discussion of operations performed or preferred by himself. He has aimed to present in convenient form a description of the operations most frequently required in general surgical practice. The general appearance of the volume makes a favorable impression. The print is large, the paper excellent, and the illustrations profuse and admirable. In many of the illustrations several colors are employed to show the anatomical structures and their relations to each other in the field of operation, and the various steps of the operations. The space given to anatomy in the text is very limited but this is more than made up for by the excellent illustrations. They emphasize to better effect what anatomy is important and exclude the unimportant. An error has crept into Figure 254, on page 415, which illustrates the operative approach to the kidney through the loin. The latissimus dorsi muscle does not overlie the posterior portion of the external oblique as shown here, but the two lie in the same plane, forming together a single layer of muscle, as shown in Figure 256 on page 423. The general excellence of the illustrations permits also a justifiable restriction of text descriptive of many of the operations. That the book is intended for the active general surgeon is shown well in the section on intracranial surgery. If the twenty-four pages allowed, only four apply to radical procedures on brain tumors and none to the surgery of the pituitary body. The remaining sixteen pages are confined almost exclusively to the general subject of craniotomy and craniectomy and their employment for middle meningeal hemorrhage, fractures of the skull, and decompression for brain tumors.

As one would expect, the practise of British and American surgeons does not always coincide. In this country the biniodide of mercury (potassio-mercuric iodide) has not "largely supplanted

corrosive sublimate in general use." Nor is iodoform any longer extensively employed. Newer methods of general anesthesia receive rather full attention, but local anesthesia is barely mentioned and spinal anesthesia not at all. General anesthesia by ether is preferred to that by chloroform, as it always has been in Dublin, and the preference thus coincides with the prevalent practice in this country. The majority of American surgeons have probably discarded most of the restrictive indications for operation on inguinal hernia enumerated by Taylor, and few will employ a drainage tube for twenty-four hours after operation. Pyelotomy for the removal of renal calculi deserves more attention than it receives, and the 'phthalein method of estimating the functional capacity of the kidney appears to be more highly esteemed by American surgeons than by Taylor, who does not mention it, and prefers Luy's urine segregator for the purpose. Aside from such differences in practice and thought, however, this work deserves, and in all probability will obtain, an encouraging reception in this country. T. T. T.

MENDELISM AND THE PROBLEM OF MENTAL DEFECT. A CRITICISM OF RECENT AMERICAN WORK. By DAVID HERON, D.Sc., Galton Laboratory, University of London. Pp. 62; 4 diagrams. London: Dulau & Co., Ltd.

As is seen by the title this is a criticism of the work done chiefly by Dr. C. V. Davenport, Director of the American Eugenics Office, either alone or in collaboration with Dr. D. F. Weeks, head of the Skillman Colony for Epileptics in New Jersey, of a paper by A. J. Rosanoff and Florence I. Orr, and lastly of a paper by A. H. Estabrook and C. V. Davenport. All these papers have been issued from the Eugenics Section and its record office, which is part of the Carnegie Institution at Washington, by its Director C. V. Davenport in the shape of bulletins by the above-mentioned authors. The criticisms are at length and go over the papers quite thoroughly. Perhaps the conclusion will best express the point of view held by the author.

"We believe that those who dispassionately consider the papers discussed in this criticism must conclude with the present writer that the material has been collected in an unsatisfactory manner, that the data have been tabled in a most slipshod fashion, and that the Mendelian conclusions drawn have no justification whatever. The authors have, in our opinion, done a disservice to knowledge, struck a blow at careful Mendelian research, and committed a serious offence against the infant science of eugenics. We shall be told, no doubt, that it is idle jealousy of the work of another laboratory. The public have common sense, and when they see

such statements as those propounded in some of these recent American papers, followed by such advice as Dr. Davenport's: 'Let weakness in any trait marry strength in that trait, and strength marry weakness,' they will apply the test of experience to such doctrine, and end by condemning wholly a science which proclaims such absurdities. Shall the stocks tainted with tuberculosis, with insanity, with epilepsy, with every defect and deformity of hereditary nature be directly encouraged to taint socially valuable stocks, healthy in mind and body, and the latter be directly told to marry weakness? When we find such teaching—based on the flimsiest of theories and on the most superficial of inquiries—proclaimed in the name of eugenics, and spoken of as 'entirely splendid work,' we feel that it is not possible to use criticism too harsh, nor words too strong in repudiation of advice, which, if accepted, must mean the death of eugenics as a science. We are confident that Dr. Davenport's advice would have been as heartily repudiated by the founder of eugenics as it is by all members of the laboratory that bears his name. The future of the race depends upon the strong mating with the strong, and on the weak refraining from every form of parenthood. Nothing short of this rule will satisfy the true eugenist."

A careful perusal of this book leaves no doubt in one's mind that the author is quite correct in his criticism. T. H. W.

THE PREVENTION OF COMMON DISEASES IN CHILDHOOD. By J. SIM WALLACE, D.Sc., M.D.L.D.S., Dental Surgeon and Lecturer on Dental Surgery and Pathology, London Hospital, Hon. Dental Surgeon, West End Hospital for Nervous Diseases. Pp. 103. London: Ballière, Tindall and Cox.

THE "motif" of the book is a plea for a diet which will stimulate physiologic mastication with all its attendant and subsequent benefits, both dental and gastric. The two main objections are that the prescribed dietary—like Fletcher's far-famed chewing—is sure to prove irksome to many; and that nutrition and digestion are liable to suffer in others. The value of the teaching could easily be tested in any institution of permanent or lengthy residence for children, where opportunity for complete supervision is afforded. With regard to other diseases than dental decay, the author's theories may be described as suggestively interesting, but it seems probable that his inferences are drawn from an insufficient medical experience. The book serves the very important function of a stimulus to thought, lest we rest too securely upon the basis of self satisfaction. J. C. G.

THE ANATOMY OF THE BRAIN. By J. F. BURKHOLDER, M.D., Professor of Ophthalmology in the School of Medicine of the Loyola University, Pp. 206; 40 plates. Chicago: G. P. Engelhard & Company.

THE purpose of this book, as set forth on the title page, is that of a "manual for students and practitioners of medicine, the brain of the sheep being selected, because of its availability and its practical identity with the human brain for laboratory use." Of the 206 pages, 113 contain the text, while the rest compose an atlas of 40 full-page plates, together with the legends.

The text consists of a running description of the parts of the brain as they are exposed, with frequent guiding references to the plates. The book is therefore a dissector and an atlas, rather than a textbook. The structures should be considered more in their relation to morphology and development. Thus, it should be explained that the lateral ventricle is but an outpouching from the third, which, in turn, is the remains of the cavity of the prosencephalon.

The plates represent with diagrammatic clearness most of the structures referred to in the text. Their artistic effect is mutilated by the guide-letters and numerals, which are of heavy black-faced type, at times a quarter of an inch in height, and by the initials of the artist, which are written in bold script.

The chief differences between the sheep's and the human brain are pointed out by Prof. Henry H. Donaldson in the introduction. The study of the architecture of the pallium of the sheep's brain can be of but little value to the medical student, except insofar as it emphasizes the greater development of the rhinencephalon in quadrupeds.

The book is of value first to comparative anatomists, and second when a study of the sheep's brain is intended as an introduction to, but not as a substitute for, that of the human brain.

P. G. S., JR.

THE SENSORY AND MOTOR DISORDERS OF THE HEART. THEIR NATURE AND TREATMENT. By ALEXANDER MORISON, M.D., F.R.C.P., Senior Physician to the Great Northern Central Hospital. Pp. 261; 12 illustrations and many tracings. New York: William Wood & Co., 1914.

THIS extremely interesting work stands as a protest against the modern tendency to base cardiac diagnosis and prognosis upon sphymographic or electrocardiographic tracings. In the 50 pages of Part I, the author gives a most satisfactory discussion of the nature of cardiac action in which he tends to emphasize the impor-

tance of the nervous system. Part II, 115 pages, concerns itself with the sensory disorders of the heart and in this discussion of the pathology, clinical history, diagnosis, prognosis and treatment of cardiac pain, the author is at his best.

The remainder of the book is taken up with a *resumé* of the disorders of cardiac motion in which the author advances a nomenclature of his own for the various varieties of arhythmia. He admits in the preface that he does not expect this nomenclature to meet with the approval of all and to the reviewer this acknowledged fault is the chief one of the book. In style and typography the book is pleasing and the illustrations are good, but the pulse tracings are certainly poor examples of the mechanical methods against which the book protests. That such a protest is not ill-timed today will be agreed in by many clinicians to whom this book will be especially interesting. O. H. P. P.

ISOLATION HOSPITALS. By H. FRANKLIN PARSONS, M.D., PH.D., Cambridge University Press, 1914.

THIS well-written book will undoubtedly be very useful to the medical profession, bacteriologists, municipal engineers, and architects, health officers, sanitary inspectors, teachers, and students.

The uses of isolation hospitals are put down as:

1. "The cure or relief of persons suffering from such diseases."
2. "The separation of such persons from the rest of the community with a view to prevent the spread of disease."
3. "To obviate the disabilities, inconveniences and primary losses which the presence of infectious sickness might entail." There value is proved by the gradually decreased death rate of the infectious diseases in the last twenty-five years.

Substitutes for hospital isolation are fully considered and advised against. "With the improvement in recent years of means of communication, with the increasing readiness to make use of hospitals in infectious illness, and with the demand for better and therefore more costly accommodations than the primitive structures and arrangements of former days, the tendency has been toward enlarged areas of combined instead of small separate hospitals." This is proved more advantageous in economy and efficiency.

The selection of a suitable site for and the design of isolation hospitals are exhaustively treated, many good suggestions made and numerous plans shown. The varieties such as movable and temporary hospitals are considered and not recommended.

Sanitary administration and extramural isolation were shown to have reduced smallpox in London from 332 per 1,000,000 to 5 per 1,000,000 in one year. T. G. A.

GENITO-URINARY DISEASES AND SYPHILIS. By EDGAR G. BALLENGER, M.D., Adjunct Clinical Professor of Genito-urinary Diseases, Atlanta Medical College; Assisted by Omar F. Elder, M.D., and EDGAR PAULLIN, M.D. Second Edition Revised. Pp. 527; 109 illustrations and 5 colored plates. Atlanta, Ga.: E. W. Allen & Company.

THE author has presented as concise a review of the subjects treated as is possible in a volume of its size and displays throughout the text the fact that he is thoroughly conversant with all the modern aspects of genito-urinary diseases. Perhaps the most notable content of the book is the "sealing-in" cure for the abortion of gonorrhea. The author claims to have cured 750 patients or 90 per cent. of cases in three to six days. This should be chronicled as *important, if true*. We are pleased to note the author's partiality to the importance and application of "vaccine therapy," but do not agree that the use of "phylacogens" is so commendable. The extent of space and discussion devoted to urethroscopy and cystoscopy we feel is disproportionate to other subjects of lesser importance. A number of misspelled words or typographical errors attracted the attention of the reviewer. We feel that the publishers have not done justice to the illustrations, which certainly are not up to the standard of a modern text-book. B. A. T.

A MANUAL OF MEDICAL TREATMENT OR CLINICAL THERAPEUTICS. By I. BURNEY YEO, M.D., F.R.C.P., Emeritus Professor of Medicine in King's College, London; Consulting Physician to King's College Hospital; Hon. Fellow of King's College. Edited by RAYMOND CRAWFORD, M.A., M.D. (Oxon.), F.R.C.P., Physician and Lecturer on Clinical Medicine to King's College Hospital, Fellow of King's College, etc., and E. FARQUHAR BUZZARD, M.A., M.D. (Oxon.), F.R.C.P., Physician for Out-patients to St. Thomas's Hospital and to the National Hospital for the Paralyzed and Epileptic, etc. Fifth Edition; Vols. I & II; pp. 834 and 846; 24 illustrations. New York: William Wood & Co.

THE author looks upon therapeutics as a study of sick people and not simply as the application of remedies to disease, and consequently prefaces his discussion of treatment in every case by an outline of the etiology, symptomatology, pathology, and clinical course of the disease insofar as these have a bearing upon the therapeusis. From these considerations he deduces his rational indications for treatment, and these he considers in turn, emphasizing only those measures which are of proved value, and not neglect-

ing the hygienic and dietetic management. For the more questionable things he states his authority without in most cases giving an expression of personal opinion.

The two volumes are divided into nine parts and fifty-eight chapters. Each chapter has at its beginning a brief outline of its contents, and important words throughout the chapter are in bold type. In addition to numerous prescriptions throughout the text there are appended to most of the chapters additional formulæ copied from various authors. In the first volume alone there appear 461 prescriptions. The last fifty-eight pages in each volume are taken up with a general index and a list of authorities for the two volumes. Taken all in all this publication is of convenient size, systematically arranged, well indexed, concisely written, and thoroughly practical. T. G. M.

TREATMENT OF NEURASTHENIA. By DR. PAUL HARTENBERG. Translated by ERNEST PLAYFAIR, M.B., M.R.C.P. Pp. 283. Edinburgh and London: Henry Frowde & Hodder & Stoughton, 1914.

THIS volume reveals the author's grasp of the whole subject of neurasthenia. The site of fatigue is no longer regarded as peripheral, a conclusion reached after much investigation with the writer's own apparatus; he at least has convinced himself that the fatigue is central.

The rest cure is heroic and only given to neurasthenics with grave debility. Diet is carefully but somewhat surprisingly treated. Milk is spoken against. Meat is highly recommended. "The neurasthenic being a weakling, requires meat to build up his blood and muscle." The amount is reduced only in the gouty, in Bright's disease and in enteritis with putrid stools. Sugar is given in considerable quantity. The best drug is strychnin in large doses and by preference hypodermically.

The management and treatment of the sexual neurasthenic is admirable and a feature is the elaborate psychotherapy. One phase of treatment is neglected: That of exercises to strengthen and tone up the abdominal muscles and organs, supplemented by abdominal support.

The book is an excellent translation of the methods employed by a successful Parisian neurologist. N. S. Y.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Effect of Nucleic Acid on the Normal Antibody.—Observations made some years ago showed that there is an increase in the natural immunity to infection following the injection of substances of the class of nucleins or nucleoproteins derived from tissues or bacterial cells. This increase was thought to be due to marked leukocytosis produced by these substances but more recent work has shown that such an explanation must be considered as incomplete. The present study of BEDSON (*Jour. Path. and Bact.*, 1914–15, xix, 191) deals with an attempt to determine what affect if any, these substances have on the normally occurring immune bodies. The first experiments confirmed the work of Leddingham in that it was found that a yeast nuclein when injected intravenously, produced a marked rise in the phagocytic index. This rise was detectable within an hour after the injection but had completely disappeared within the course of twenty-four hours. Several other preparations were similarly tested with reference to their power to raise the opsonic index. These included: (1) sodium nucleinate (Merck), (2) a yeast nucleic acid (Boehringer), and (3) a preparation of pure tissue nucleic acid supplied personally. Following the use of some of these, no rise in the phagocytic index was obtained, which tends to confirm the idea advanced by Gay and Robertson, who believe that these preparations of nuclein and nucleic acid, which act as antibodies, are able to do so owing to the presence of some protein impurity obtained in the first instance from the tissue or bacterial cells from which the acid was derived. The increased opsonic activity of the serum is readily determined by heating for thirty minutes at 56° C. and by diluting with normal salt, from which it would appear that there

is no increase in the thermostable opsonin normally present in the serum. If this is the case, it may be possible that the injection of these substances results in an increase in the complement content of the serum and that this is responsible for the increased opsonic power of it. Some evidence in favor of this view has already been advanced.

The Pressure Curves in Cases of Auricular Fibrillation.—WIGGERS (*Arch. Inter. Med.*, 1915, xv, 77) describes the instruments which have been used by him to study in detail the pressure changes in the auricles, ventricles and aorta during auricular fibrillation. The instruments used are essentially optically recording manometers of high vibration frequency and a photokymograph by means of which records of any length can be obtained. In experimental animals it was found that the auricular contractions in themselves produce no intra-auricular pressure waves. The intraventricular pressure curves show that the ventricle contracts at a very irregular rate, the height of the pressure being determined largely by the interval between the contractions. Thus, when the pace is set too rapidly, there results a series of inefficient systoles which may result in a fall of the arterial pressure and dilatation of the ventricles. These contractions are often not strong enough to open the aortic valves and hence such contractions are not accompanied by any audible sound. This is of importance in the clinical auscultatory explanation of the ventricular rate. The aortic pressure is influenced only by these systoles which are capable of raising the intraventricular pressure above the arterial diastolic pressure and hence it follows that the amplitude of the arterial waves depends upon the strength of the ventricular contraction and the diastolic pressure. The amplitude, therefore, of the arterial pulse is not a suitable criterion of the strength of the heart beat in these cases. The curves show that the vigor of the ventricular systoles is largely governed by the time relation between contractions.

Studies on the Oppler-Boas Bacillus.—This bacillus was first described in 1895; since then practically no work has been done to determine its exact place in the bacteriological world. Numerous observations have confirmed the fact that these bacilli are essentially associated with malignant conditions in the stomach, but they may occur in benign ones. The bacillus doubtless belongs to the so-called "acidophile" group, the members of which produce lactic acid and are capable of growth in media which are detrimental to most other organisms. The best known representative member of this group is the B. bulgaricus, which was first described in 1905. The present work of GALT and ILES (*Jour. Path. and Bact.*, 1914–15, xix, 239) consists of the study of three strains of Oppler-Boas bacillus which were isolated from three cases of cancer of the stomach, which showed the presence of lactic acid and the absence of hydrochloric acid. Cultures were best obtained by sowing them in whey with subsequent transplantation for three days' incubation to plates from which characteristic colonies could be transferred to litmus milk. These strains were then compared under standard conditions with a known culture B. bulgaricus, to which the resemblance on morphological and cultural grounds is so close that the description of one applies equally well to

the other. Full details of these characteristics are given. True dichotomy was observed in both organisms which strongly suggests that the B. bifidus is also identical with them. Galt and Iles conclude from their evidence that the Oppler-Boas bacillus is not an organism *sui generis*, but is identical with the B. bulgaricus and that in cases of cancer of the stomach it is the absence of hydrochloric acid that permits of the growth of the bacillus and that lactic acid is formed as a result of the activity of this organism.

A New Malaria Parasite.—J. W. W. STEPHENS (*Annals Trop. Med. and Parasitol.*, 1914, viii, 119) describes what he believes to be a new species of malarial parasite, which he designates Plasmodium tenue. His observations were made from one stained smear sent to him from Pachmari, Central Provinces, India. The parasite is (1) extremely ameboid (judging from the stained specimen). Thin processes often extend across the cell or occur as one or more long tails to more or less ring-shaped bodies, giving the parasite peculiar fantastic shapes, like an irregular web or mesh, when the processes are multiple; (2) the cytoplasm is always scanty, the pseudopods being delicate or thin. The parasite has but little bulk or density. While forms resembling "rings" do occur, yet, owing to the abundance of all kinds of irregular forms, it is difficult to find typical signet rings. Laterally applied parasites also occur, but in them the chromatin is not dot-like, as is usual in the malignant tertian, but practically always rod-like; (3) the nuclear chromatin is out of proportion to the volume of the parasite. It takes the form of rods or bars, strands, curves, forks, patches; the occurrence of chromatin in dots, as in the ring forms of other species, is rare. In the web-like protoplasmic processes mentioned above, there may be seen several chromatin strands, and not uncommonly one observes a minute dot of chromatin some way from the parasite, or between two processes, of the parasite, though the protoplasmic process connecting it with the main mass or masses is so thin as to be invisible. The chromatin masses are frequently angular, the angles jutting into the points at which an ameboid process is given off. Abundance of, and marked irregularity in the distribution of, the chromatin masses are characteristic of this parasite. (The value of the description is much enhanced by a beautiful colored plate, showing numerous parasites.) The new parasite differs from the malignant tertian parasite (Pl. falciparum) in the following particulars: (1) Its ameboid activity. In the case of the malignant tertian parasite a certain amount of ameboid activity is observable, giving rise to "star-fish" shapes and to somewhat irregular or even bacillary forms; but the activity is not comparable to that of Pl. tenue, which has for this reason a most strange and peculiar appearance; (2) in the abundance and irregularity of nuclear matter. Signet rings are rare. From Pl. vivax it is distinguished (1) by the fact that its bulk is much less (*i. e.*, it is a smaller parasite); (2) its ameboid processes are far more delicate; (3) the chromatin shows a relative abundance, an irregularity and a peculiarity of arrangement (*e. g.*, strands, bars and rods) not seen in Pl. vivax; and (4) typical signet rings are exceedingly rare or absent. The author was unable to determine definite swelling of infected erythrocytes; in some instances it was present, in others the infected cells were

diminished in size. There seemed to be no rule. Schuffner's granules were found in one infected red cell, which contained a parasite considerably larger than any others encountered. Although Stephens could detect no pigment in this particular parasite, it was otherwise indistinguishable from a simple tertian parasite.

Naso-oral Leishmaniasis (Espundia) Originating in the Anglo-Egyptian Sudan.—J. B. CHRISTOPHERSON (*Annals Trop. Med. and Parasitol.*, 1914, viii, 485) reports two interesting cases of leishmaniasis originating in the Anglo-Egyptian Sudan. Naso-oral leishmaniasis, known as espundia, has hitherto been described only in South America (Peru and Brazil). The case reported by Christopherson corresponds clinically with the descriptions of espundia. In the ulcers typical Leishman-Donovan bodies were found, though they were very few in number. Media on which the kala-azar organisms grew readily were inoculated with scrapings from the ulcers, but no growth occurred. The case of cutaneous leishmaniasis (Oriental sore) reported also originated in the Sudan, the first recorded from this district, in which kala-azar is of frequent occurrence.

SURGERY

UNDER THE CHARGE OF

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Observations on Myeloid Sarcoma with an Analysis or Fifty cases.—STEWART (*Lancet*, Nov. 28, 1914, 1236) says that there is no subject in the whole range of surgical practice where the coöperation of surgeon and pathologist is more necessary than in the case of myeloid sarcoma. Not only the extent of the operation but the ultimate prognosis depends finally on the histological diagnosis, although in most instances it is possible to say, from the naked-eye characters alone, whether or not one is dealing with a case of this kind. On the other hand, a perusal of the literature shows that errors in diagnosis may be made even where the growth is submitted to microscopic examination, and this is generally due to mistaking a malignant giant-celled for a myeloid sarcoma. Although it is the usual teaching nowadays that these growths (myeloids) are of very low malignancy, there still seems to be an unwillingness on the part of many surgeons to treat them by local excision, and this is undoubtedly due, as already indicated, to the fact that in the past, cases of so-called myeloid sarcoma have been reported

in which death with visceral dissemination occurred at a longer or shorter period after operation. These 50 cases have been investigated from both the clinical and pathological stand-point, but special attention has been paid on the one hand to the question of prognosis, and on the other to the minute anatomy of the growths. Stewart divides giant-celled sarcomata into: (1) the myeloid sarcomata, myelomata of some authors; and (2) the malignant giant-celled sarcomata. Myeloid sarcoma is locally malignant only and does not undergo dissemination. It is to be clearly distinguished, both clinically and pathologically, from malignant giant-cell sarcoma, in which death with visceral dissemination is the rule, even after the most radical operative treatment. The histological diagnosis is based on the morphological characters of the giant cells, especially as regards their neuclei. In myeloid sarcoma the latter are numerous, uniform, small, and without mitoses; in malignant giant-cell sarcoma they are few, sometimes single, irregular, and often very large, while mitotic figures are frequent. After investigating this comparatively large series of cases, and from a study of the literature, Stewart feels bound to advance a strong plea for the conservative treatment of myeloid sarcoma. Especially would he advocate thorough curettage as the operation of choice in the first instance in suitable cases; failing this, a local resection of the growth. Amputation should be the last resort, and only after the failure of less radical measures. An accurate histological investigation of the tumor is in all cases essential.

Acute Emphysematous Gangrene.—SWAN, JONES and MCNEE (*Lancet*, Nov. 14, 1914, 1160) say that since the commencement of the war some 2000 cases have been admitted to the Royal Herbert Hospital, but this disease has only appeared in the last fortnight. In the three cases reported were found spore-bearing organisms identical morphologically with the bacillus of malignant edema. The diagnosis of "malignant edema" in these cases, however, rests as much on the clinical appearances as on the bacteriological findings. The following diagnostic points are emphasized: (1) The blackish-brown, almost charred appearance of the wound; (2) the abundance of a thin, brown-colored serous discharge, in which microscopically much granular debris but comparatively few pus cells could be recognized. Great numbers of other pathogenic organisms were present in all three cases in addition to the spore-bearing bacilli; (3) the curious heavy, penetrating odor from the wound; (4) the skin surrounding the wound became of a slate-blue color. Blisters containing brownish fluid were present over the area of dark skin in the case in which the gangrene had spread; (5) fine emphysematous crepitations could be made out in the tissues surrounding the wound; (6) marked toxemia accompanied the disease in the two fatal cases, but it is noteworthy that in both of these consciousness was unimpaired until a minute or two before death. With the occurrence of the disease active measures must be adopted as soon as the bacteriological evidence is forthcoming, first to isolate the patient from other surgical cases and then to attack the wound. In the first cases the condition was hopeless from the onset of the spreading gangrene, and in the second amputation well above the wound was performed at once owing to the extensive injury to the knee-joint. In the

third case the patient's general condition was such that it was decided to attempt in the first place to save the limb, especially as any operation would have to be performed through infected tissue. When it can be carried out, free and extensive incisions into the area with thorough swabbing with peroxide of hydrogen and permanganate solution should be used, and the writers are inclined to recommend this in preference to carbolic acid, because the organisms are anaërobic. Dressings soaked with hydrogen peroxide were applied very frequently. At the same time large quantities of saline should be given by the rectum and subcutaneously.

The Treatment of Osteomyelitis: Observations on Ninety-seven Cases, with the End-results.—Simmons (*Surg., Gynec., and Obst.*, 1915, xx, 129) says that in children with pain in a limb and evidence of toxemia, always consider osteomyelitis. Operate early even if the symptoms are rather vague. If the diagnosis is incorrect practically no harm is done while if correct a great deal of suffering may be avoided. In acute cases, open to the medulla and pack the wound. The prognosis is good. The treatment and prognosis varies of necessity somewhat in these early cases but in general the earlier the operation the better the prognosis. In cases where bone destruction has taken place, seen less than three months after the onset of the disease, perform subperiosteal resection when possible. The prognosis is good. In chronic cases of bone abscess of less than one year's duration, drain and pack. The prognosis is good. In chronic cases with bone destruction of less than one year's duration, remove the sequestrum and pack. The prognosis is good. In old chronic cases, either with bone destruction or of the bone abscess type, remove necrotic areas and drain. Try to obliterate the cavity with flaps of living tissue. If this cannot be done either use bone wax, pack or sterilize the cavity, allow it to fill with blood-clot, and close without drainage. The prognosis, if the cavity can be obliterated, is fair, otherwise poor. The treatment when such bones as the pelvis are involved is unsatisfactory and the prognosis problematical. When in old chronic cases the shaft of a long bone is badly diseased the possibility of resection of the entire shaft with bone transplantation is resorted to.

Experiences with Nail Extension.—Grabowski (*Deutch. Ztschr. f. Chir.*, 1915, cxxxii, 529) reviews the experiences of various surgeons wtih this method of extension and reports 19 fractures of the lower extremity treated by nail extension in Garrè's clinic at Bonn. They were for the most part simple fractures, a number having united with deformity. The following technique was observed: After thorough disinfection and painting of the skin with iodin, a nickel-plated nail or gimlet was driven into the bone. The free ends were wrapped around with iododform gauze, covered by a sterile metal cap and the whole protected by a gauze bandage. For extension from the calcaneus a single perforating nail is employed and for the femoral condyles a nail is used on each side, because it diminishes the danger of tearing away the bone at the epiphyseal line. In fractures the nail is passed near the junction of the epiphysis and diaphysis and in fractures of the leg through the calcaneus, in order to avoid danger to the joints. Control during the treatment is maintained by the Roentgen-ray and measurements.

In most cases local anesthesia was employed, light general anesthesia being employed only in especially painful cases. The experience at the Bonn clinic is favorable to nail extension and shows it to be very effective. Its superiority over other methods of extension, especially in complicated and old fractures with deformity, is beyond doubt. It cannot be considered, however, as the method of choice because of the dangers associated with it. Grabowski considers it as an open operation with its possibilities of danger. One case resulted in a severe infection extending from the nail. In the Bonn clinic nail extension is reserved for especially appropriate cases, those in which the Bardenheuer method fails or its employment seems without hope of success. Nail extension has given brilliant results in advanced consolidation with considerable shortening and bad position of the fragments. It is valuable in complicated fractures with marked overlapping of the fragments and extensive injury of the soft tissues. The extension can be applied immediately with proper treatment of the wound, with far better prospects than formerly of good functional results. A third indication for nail extension is to be found in very severe fractures of the leg near the ankle-joint, in which there is not sufficient room for the application of the adhesive plaster extension. The indications for this method of extension, however, were very limited in the Bonn clinic. The technique should be observed closely and infection guarded against carefully. Only under these circumstances with a proper choice of cases and in experienced hands, should the method be used.

The Gross Anatomy of the Human Prostate and Contiguous Structures.—Lowsley (*Surg., Gynec., and Obst.*, 1915, xx, 183) says that this report is based upon a study of two hundred and twenty-four prostate glands from patients varying in age from one month to seventy-nine years, most of which were obtained from routine autopsies conducted by the pathological department of Bellevue Hospital. These specimens have been studied in gross, in sections, and microscopically, both in serial sections and in sections taken at random. It has seemed wise to consider in this communication only the gross characteristics of the structures at the neck of the bladder, as relationships at this complicated area are of the utmost importance to the genito-urinary surgeon. The following interesting facts are deduced from the study: The width of the prostate in every instance is greater than the height, always less than the length. The prostate develops very slowly until puberty, at which time it increases enormously in size, assuming proportions which are twice those previous to this period. It reaches a maximum size during the third decade. One out of every four specimens observed shows an obstruction of greater or less extent at the orifice of the bladder. Asymmetry of the trigonum vesicæ frequently occurs (26.3 per cent. of Simmons' cases). The upper portion of the posterior urethra continually lengthens from birth until death. The seminal vesicles and the lower end of the vasa deferentia are enveloped in a triple-layered fascia, which is of great importance surgically. Enlargement of the seminal vesicles occurs in one-third of the cases over twenty years of age, the right being affected three times as often as the left. The ejaculatory ducts rarely, if ever, open into the utriculus prostaticus.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Pyorrhea Dentalis and Alveolaris.—Bass and Johns (*Jour. Amer. Med. Assoc.*, 1915, lxiv, 553) say that pyorrhea dentalis and alveolaris is practically a universal disease, which leads to the loss of the teeth by a long suppurating process. All people have it sooner or later. It begins in early adult life or earlier. They believe that the specific cause of the disease is Endameba buccalis and possibly other species which infect and destroy the peridental membrane. The pyorrhea results largely from the secondary infection. The demonstrable emdamebas can be destroyed by giving $\frac{1}{2}$ grain of emetin hydrochlorid hypodermically for three to six successive days. Apparently equal endamebacidal effect is produced by two or three alcresta ipecac tablets taken by mouth three times a day for four to six successive days. This form of ipecac does not cause nausea, but there is frequently more or less abdominal discomfort produced by it and also some looseness of the bowels. The lesions require variable lengths of time to heal, but many could not reasonably be expected to heal in less than several weeks or months. The treatment must be repeated from time to time until the lesions all heal. Injecting ipecac or emetin into the worst lesions ought to be of service and can be carried out by patients in many instances. Rinsing the mouth thoroughly with a solution of fluid extract of ipecac is believed to protect, to some extent, against reinfection, and actually cures the disease in its earliest stage in some instances.

The Effect of Intravenous and Intraspinal Treatments on Cerebrospinal Syphilis.—Draper (*Arch. Int. Med.*, 1915, xv, 16) reports a series of 25 cases of syphilis of the cerebral nervous system grouped with especial reference to the predominating symptom or symptoms. These twenty-five patients were all treated intensively for active syphilis. All but one received combined intravenous and intraspinal injections. Mercury and potassium iodin were also used, but the chief reliance and interest were centred on the action of salversan, neosalvarsan, and salvarsanated serum. Most of the patients were treated intravenously at weekly intervals with doses of salvarsan varying from 0.3 to 0.6 grams, or neosalvarsan in full doses. Salvarsan was the drug of choice and was changed for neosalvarsan only when the patient had an anaphylactic reaction. The usual technique in the preparation of doses was observed. Intraspinally most of the cases received 30 c.c. of 50 per cent. or from 20 to 25 c.c. of full-strength serum, separated by centrifugalization from blood withdrawn forty minutes after the intravenous dose of salvarsan. The serum was heated to 56° C. and was introduced intraspinally the same day. Lately

several patients have been bled before the intravenous dose, and then salvarsan up to a milligram added *in vitro* to the serum. This mixture was heated to 37.5° C. for forty minutes, and then 56° C. for half an hour. No serious symptoms followed any of the injections. Clinically, very marked improvement occurs in all groups of cases. In the spinal types pain is usually relieved; ataxia helped in most instances, and not very markedly in a few. The bulbar types and those with fairly pronounced psychic disturbance depending perhaps on meningeal irritation, show marked improvement in symptoms as well as in spinal fluid. The more definite psychic disturbances also may clear up completely, but their spinal fluids cannot in every case be brought to normal. The cell-count has almost always been reduced in them but the Wassermann test rarely disappears below 0.3 c.c. In some cases, especially those treated with serum salvarsanized *in vitro*, transient numbness in the feet has appeared; in other cases a slight failing in general robustness which may be an arsenic effect; and in several instances rather severe pains following the intraspinal injection have been seen. In two cases there has been a sudden increase in ataxia following a period of definite improvement. Notwithstanding these undesirable features, the improvement in symptoms in almost all cases is of such striking nature that the method should be given a most careful and thorough study by numerous observers. It is, however, a procedure which must be carried out with the greatest attention to the detail of technique in all its steps, otherwise serious symptoms may be induced. At present there is sufficient evidence to show that it is unsafe to give more than two, or at most three, consecutive injections of serum to which salvarsan has been added directly. In no case should more than 0.0005 gram be added. On the other hand, apparently any number of intraspinal injections may be given with impunity when serum salvarsanized *in vivo* is used. In those cases which do well the rapid and satisfactory improvement may lead to a premature cessation of treatment. But with our present knowledge of the significance of syphilitic serological reactions, so long as the spinal fluid or blood gives a positive Wassermann test, the case must be looked on as one potentially capable of relapse. Consequently, no matter how well the patient feels and seems to be, treatment must be continued unremittingly until the laboratory tests are persistently negative.

Sensitized versus Non-sensitized Typhoid Bacteria in the Prophylaxis and Treatment of Typhoid Fever.—GARBAT (*Jour. Amer. Med. Assoc.*, 1915, lxiv, 489) reports a series of 17 consecutive cases of typhoid fever treated with sensitized vaccine. In the majority of instances treatment was begun in the second week of the disease when the diagnosis was definitely established. Of this series only one patient died who developed a large, deep spreading abscess of the thigh and scrotum requiring operation. Four patients had relapses. Only in two of the 17 cases did the temperature subside acutely, reaching normal forty-eight to seventy-two hours after the vaccine inoculation; in the great majority the temperature did not go any higher but began to show remission, coming down to normal gradually. On the whole, the impression was gained that the inoculated patients ran what might be termed mild courses with comparatively few complications.

Garbat believes that the treatment of typhoid fever by sensitized typhoid bacteria offers a more rational therapy from an immunologic point of view that by the ordinary non-sensitized vaccine. The repeated inoculation of large doses of sensitized vaccine even in very sick patients, was not attended by any harmful effects or a distinct negative phase; the general course of the disease seemed milder and the complications less; the occurrence of a crisis in the infection took place in a small percentage of cases, the improvement usually being gradual. He also suggests that perhaps more striking results will be attained by a larger number of smaller doses more often repeated.

Splenectomy in Primary Pernicious Anemia.—ROBLEE (*Jour. Med. Assoc.*, 1915, lxiv, 796) in the summary of his article states that primary pernicious anemia is probably due to a toxin of bacterial, chemical or parasitic origin, and in some cases there is an increase of the unsaturated fatty acids. The spleen seems to exercise an influence favorable to the elaboration of these substances. These toxins appear also to cause a hyperemia of the splenic pulp because of changes in the blood-vessels, which cause the blood to be poured directly into the pulp. The presence of the spleen seems to cause a diminution in the amount of the total fats and cholesterins of the blood which are antihemolytic. For these theoretical reasons, and because of the numerous cases on record in which a cure has been obtained in Banti's disease, which is closely related to pernicious anemia, splenectomy appears to be indicated in these and the closely associated anemias. Removal of the spleen either in sickness or in health does not effect the patient injuriously. The operative mortality is not high even in very weak patients. A rapid and striking remission of all symptoms appears, the change in the blood picture coming quickly and quite certainly. It is as yet too soon to know whether or not any patients will be permanently cured, but it is quite probable that a large percentage will succumb to the disease within a few months after operation. Other methods of treatment should be combined with splenectomy, as more than one factor is doubtless at work in these cases. It will certainly prolong life, and in our incomplete knowledge of the etiology of this disease and the certainty that death will come under every other method of treatment, he believes that these patients should be offered this additional chance of recovery. We must remember that some patients have been reported symptomatically well at the end of nine months, even though the blood still showed the characteristics of pernicious anemia.

The Treatment of Syphilis with Copper Salvarsan.—FABEY and SELIG (*Münch. med. Wchnschr.*, 1915, lxii, 147) write concerning copper salvarsan which is a combination containing about 24 per cent. of arsenic and 11.6 per cent. of copper. According to the authors this preparation has certain advantages over salvarsan and neosalvarsan. They claim that smaller doses of arsenic are required to cause disappearance of the symptoms and in consequence of these smaller doses of arsenic the injections can be given more frequently. They found that patients bore the injections well and no untoward symptoms were noted. The chief objection to its use is that the preparation of

the solution is very complicated and can be carried out only in the hospital, therefore cases cannot be treated on the ambulatory plan which is the aim of salvarsan therapy. They claim that copper salvarsan is efficient in all three stages of syphilis and influences syphilitic symptoms quickly and positively. The effect on the Wassermann reaction, however, is not so marked as with the older preparations of salvarsan.

PEDIATRICS

UNDER THE CHARGE OF

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Subcutaneous Injections of Antitetanic Serum.—J. COMBY (*Brit. Jour. Child. Dis.*, 1915, xii, 1) describes three cases of tetanus in children cured by the subcutaneous injection of antitetanic serum. He reviews much of the literature pertaining to the intracerebral and intraspinal methods of administering the antitetanic serum, and shows numerous successes following each of the different methods. The first case of the author's series was a boy, aged eleven years, in whom tetanus developed nineteen days after the injury. Two hundred c.c. of antitetanic serum were used subcutaneously in eight days followed by recovery and by serum arthralgia and urticaria eight days after the last injection. This case serves to show the harmlessness of large and repeated doses of antitetanic serum and the success of large doses in young persons. The author, however, prefers preventive serotherapy, and believes that all wounded in the streets or in battle should be given a preventive dose of from 10 to 20 c.c. of antitetanic serum. The second case occurred in a boy, aged thirteen years. Eighteen days following injury tetanus made its appearance. Recovery occurred after subcutaneous injection of 10 c.c. of serum daily for five successive days, showing that success may follow when relatively moderate doses are given. The third case occurred in a boy, aged twelve years, in whom the tetanus did not appear until three weeks after the injury. Recovery followed one subcutaneous injection of 40 c.c. serum. With a long incubation period the course of the disease is long and the prognosis good. With a short incubation period the course is short and the prognosis almost always fatal, irrespective of the serum therapy usually.

Blood-pressure Estimation in Children.—MELVIN and MURRAY (*Brit. Med. Jour.*, 1915, No. 2833, 669) offer an excellent discussion of the technic and results in blood-pressure estimation in children. Blood-pressure, clinically is a more or less constant pressure—the diastolic pressure—on which is periodically imposed an additional pressure—the systolic pressure. Any instrument is inaccurate which is indefinite in this indication it is designed to give, such as maximum oscillation,

etc. The auditory method is simple, determinate and accurate, especially in children. The apparatus consists of an ordinary mercury manometer, an armlet about 8 cm. broad, some form of filler and an Oliver tambour with strap attachment which leaves the observer with both hands free. With the armlet snugly fitted to the upper arm, the tambour strapped lightly over the artery at the elbow and the ear pieces fitted to the ears, one hand palpates the radial pulse and the other manipulates the compressor. As the pressure is being reduced the observer hears the onset of the first, sharp, clear sound. This indicates the systolic pressure on the manometer and occurs before the pulse is felt in the radial artery. The point at which the loud clear sound becomes dull and diminished in intensity is the indication of diastolic pressure. Investigations were made on 40 children of an average age of 9.5 years. These were all normal children. The average systolic pressure was found to be 108.1, only slightly lower than in adults which was found by the same method to be 111.8. The diastolic pressure in the children was 72.4 as against 65.7 in the adults, and the pulse pressure was 35.7 as against the adult pressure of 46.0. These readings for children are definite and reliable and constitute a sound basis for the study of pathological variations.

Bacteriology of the Urinary Tract in Children.—Ross (*Lancet*, 1915, clxxxviii, 654) gives the results of a bacteriological examination of 106 catheter samples of urine. A series of 19 catheter specimens from normal children were also examined and 11 were found sterile after seventy-two hours incubation and 8 grew an organism which was invariably a white staphylococcus. This coccus is probably present in that part of the urethra inaccessible to outside cleansing. In the infections by the Bacillus coli Ross divides the cases into those entirely latent or with mild symptoms only, such as slight pyrexia, and showing a few leukocytes in an acid urine and the class of cases with frank pyuria with symptoms of cystitis or pyelitis. Most of the cases investigated belonged to the first class. Out of 43 cases of this type of infection 36 were females and Ross favors the view that infection is from without and due to a direct passage of organisms from the anal orifice to the vulva and thence upward. This view will not cover all cases, most of which were suffering from acute summer diarrhea. Given an impaired resistance the colon bacillus might easily gain entry to the bladder by direct extension in the fema'e. The colon carrier is distinct from the pyuria cases with their very abundant leukocytes. Out of 40 cases of colon infection examined, only one showed a true pyuria. The autogenous vaccine treatment on three cases of pyuria showed a diminished amount of pus and some clinical improvement but the bacilluria persisted. In certain cases of acute enteritis complicated by edema the majority had a colon bacilluria but there was no obvious connection between the bacilluria and the edematous state. Staphylocci alone were isolated twenty-five times from pathological urines. Their value as etiological factors in pathological conditions is discounted by the fact that they can be cultivated from control urines, their low degree of virulence and the great diversity of pathological states in which they are found.

OBSTETRICS

UNDER THE CHARGE OF

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The Absorptive Power of the Genital Tract During the Puerperal Period.—AHLFELD (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) cites a classic case of Walthard, where a woman, aged forty-two years, whose last labor had been nineteen years previously, stated that she had suffered from fever on this occasion during the puerperal period. She suffered greatly from an adherent retroflexed uterus, and was operated upon. No fever developed after the operation, but peritonitis occurred, with death on the fifth day. At autopsy, bacteriological examination of the interior of the uterus, and also of the pus from the abdominal cavity, was made, showing the presence of Streptococcus pyogenes, Bacillus coli communis, and the bacillus of malignant edema. There was every reason to believe that these germs had remained in this patient's uterus for nineteen years, in the form of spores, and that they had developed at the time of operation. The writer has also reported a case where a primipara gave birth to a child of very moderate size, after an entirely normal labor. The placenta was delivered by expression, when it was found that the vagina was closed by a hematoma as large as a fetal head. The pulse during labor had been 64, the temperature 97.5°. A record was made of the temperature for fourteen days, morning and evening, and on the evening of the fifth day the temperature rose to 103°. A vaginal douche was then given daily. As every precaution had been taken in labor, the blood retained in the vagina became infected from germs in the body of the patient not introduced from without. Ahlfeld concludes from his observations that at no time in pregnancy, labor or the puerperal period, does the absorption of pathogenic material go on simultaneously from the vagina to the uterus. Independently of the size of the uterine cavity absorption from the contracted uterus is lessened and from a relaxed uterus increased. On the third, fourth and fifth days of the puerperal period absorption from the inner surface of the uterus is most active. From the sixth day on this steadily diminishes, especially when the uterus undergoes prompt involution. The most rapid and abnormal absorption is seen in cases where after the sixth day the uterus remains unusually large. These observations evidently have a practical bearing of considerable value on the occurrence of puerperal septic infection.

Purulent Peritonitis at the End of Pregnancy from Infection of a Placenta Previa.—FRANK (*Monatsch. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 2) describes the case of a multipara who, during her last pregnancy, suffered greatly from disturbance of the stomach, with tenderness over the epigastrium. Examination by a physician showed pregnancy at five months. Life was felt naturally, but the

patient suffered from severe pain in the right side which extended up to the right breast. About a month later the amniotic liquid escaped, followed by symptoms of peritonitis, chills, and pain in the abdomen, for which the patient was sent to hospital. Examination showed that the cervix had not been obliterated, but could be found high in the right side of the pelvis, and very thick and dense. The tip of the finger only could be introduced through the external os. The uterus was contracted tetanically. No fetal tear could be felt. Heart sounds could be heard on the level of the umbilicus. As there was no active pain the patient was given morphin to secure rest. Pain gradually developed, accompanied by vomiting of bile-stained material. After some hours there was sudden vaginal hemorrhage so severe that the patient collapsed. On examination the vagina was full of blood and the cervix unaltered, but one finger could be introduced through the cervix. When the finger was carried, with difficulty, through the cervix it came upon a mass of rather tough tissue which could scarcely be made out. Fetal heart sounds could no longer be heard. On opening the abdomen purulent peritonitis was found, and Douglas's cul-de-sac was filled with purulent fluid. The intestines were adherent and greatly injected. The child was still living and was quickly extracted. The heart sounds were weak, but the child could not be revived. The appendix was removed, the uterus encircled by a constricting band, and the peritoneum closed around the stump. Although the patient was severely shocked she made a final recovery. On studying the specimen it was seen to have been a central placenta previa, with masses of fibrin and thrombi, showing that infection had occurred at the site of the placenta previa and in its tissue.

Malaria Complicating the Puerperal Period. — Solomons (*Jour. Obst. and Gynec. Brit. Emp.*, September, 1914) describes the case of an apparently healthy primipara with normal pelvis, and the fetus in breech presentation. The patient had lived for some time in India. Labor developed with the breech impacted high in the pelvis. It was necessary to extract the child, which was done with great difficulty. There was extensive laceration of the perineum into the rectum. The lacerations were immediately closed. The temperature rose to 102°, and a pulse of 120 developed on the fourth day. Bacteriological examination was negative, so far as the contents of the uterus was concerned. The urine contained a slight amount of albumin but no pus, and the chest sounds were normal. Blood was taken from a vein in the arm, and another examination was made for the malarial parasite, which was present. Quinin bisulphate, 10 grains three times daily, was given, which brought the temperature to normal after six days. It so remained for nine days, and the patient had been up for two days, when on the thirtieth morning the temperature again arose, and on the following day was 103°. Quinin was again given, and the final recovery of the patient followed. No mention is made of the fetus, and evidently the blood of the child was not examined to determine the presence of the malarial parasite. The reviewer has observed severe malarial intoxication occurring after spontaneous labor in the wife of a coal miner, who had contracted malaria when living in the vicinity of a semi-stagnated creek and pool. On the fourth day after

labor the temperature rose to 104°, accompanied by severe chills. Microscopic examination of the blood showed the characteristic parasite. The free use of quinin was followed by the patient's gradual and complete recovery. During the height of the malarial paroxysm the child was not allowed to nurse, the breasts were evacuated by the breast-pump, and the child was fed artificially. When the mother became convalescent the child was able to resume nursing, and the mother and child ultimately made a complete recovery.

A Case of Adeno-cystoma of the Labium Majus, of Fetal Origin.—GERLICH (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 2) from the hospital in Przemysl reports the case of a women, aged twenty-four years, who gave a history of three spontaneous births. During the first confinement a small tumor in the right labium was noticed which had grown slowly but steadily since that time. It had evidently become sufficiently large to cause inconvenience, and its removal was desired. On examination, the pedicle of the tumor extended the length of the right labium majus. The tumor was covered with unaltered integument, and over it passed some large veins. On examining the tumor with a detached light, it seemed to contain an almost clear fluid resembling that in hydrocele. There was no fluid in the labium itself, and on pressure the cystic tumor did not diminish in size. There was no abnormality in the surrounding tissues. The operative procedure consisted in dissecting out the cyst under anesthesia and in uniting the borders of the wound by stitches. Primary union occurred in eight days. On microscopic study of the tumor it was found to be a papillary adenoma with a sufficient mixture of fetal tissue to show that it was of fetal origin. Similar cases have been reported by Weber, Ludwig Meyer, Veit, Bluhm, and others. Illustrations showing the microscopic study of the tumor are included in the paper.

The Diagnosis of Uno- or Duovular Twins Before and During Labor.—AHLFELD (*Monatschr. f. Geburtsh. u. Gynäk.*, 1915, Band xli, Heft 2) believes that the question as to the origin of twins from one or two ova can be settled by diagnosis during labor. When after the birth of the first child the second engaging in breech presentation is of the opposite sex to the first, the twins are du-ovular. It is observed that twins of different sex are never produced from one ovum ouly.

The Etiology of Chorio Gravidarum.—ALBRECHT (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, Band lxxvi, Heft 3) describes the case of a young primipara who during pregnancy was taken with disturbance of the nervous system. Choreic movements were present in the upper extremities, without pain, becoming worse at evening and ceasing during the night. An examination of the patient showed the muscles to be poorly developed and the fatty tissue in moderate quantity. There was no edema. Sensibility was intact. The movements of the right hand and also of the right lower extremities, the facial muscles, and the muscles of deglutition, were irregular and incoördinate. The reflexes were fairly active, and a diagnosis of chorio-gravidarum was made. For sixteen days the patient was treated with bromides, quinin, and antipyrin, without result. A trial was then made of normal preg-

nancy blood serum, given by injection into the gluteal region, the dose being 20 c.c. Immediate improvement followed, and there was no relapse during the pregnancy. He also describes the case of a girl, aged sixteen years, in whom menstruation had not yet been established, who had well-marked chorea, with difficulties in speech and in swallowing. After the patient had been in hospital for a few days menstruation appeared and the chorea became intensely violent. When the period gradually ceased the patient began to improve and made a good recovery. There seemed to be a definite relation between the function of menstruation and the chorea.

GYNECOLOGY

UNDER THE CHARGE OF

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The Coincidence of Gall-stones and Gynecologic Diseases.—In a paper presented before the Southern Surgical and Gynecological Association, PETERSON (*Surg., Gyn.. and Obst.*, 1915, xx, 284) takes up the questions of the frequency, significance, and treatment of gall-bladder conditions occurring coincident to some pathology of the lower abdomen or pelvis, for which latter the patient has primarily come to operation. He said that the day of the small incision in dealing with intra-abdominal pathology is a thing of the past, since through such an incision it is often impossible to discover important subsidiary conditions, which may subsequently give rise to more trouble than the one for which the operation was performed. He thinks, therefore, that unless special conditions contra-indicate it, every abdominal incision should be large enough to permit the introduction of the operator's entire hand, for thorough exploration of the abdominal cavity. It has come to be pretty well recognized, Peterson says, that under ordinary circumstances the appendix should be routinely removed when the abdomen is opened for any purpose, in order to stall off the possibility of future trouble in that organ. He now wishes to raise the question, whether the gall-bladder does not offer as important an organ for at least routine examination during every pelvic or abdominal operation, in the absence of pus, adhesions, or other special contra-indications. Personally, he firmly believes that it does, having been gradually brought to this viewpoint by the relatively large number of cases in which he has found stones, or other distinct pathological conditions in the gall-bladder, in patients whose primary symptoms were located in the field of strict gynecology. His paper is based on a series of 1066 such cases, in all of whom the gall-bladder was palpated during the course of a gynecologic laparotomy, and in something over 12.5 per cent. of whom gall-stones were discovered, although in no instance has a gall-stone history been in the foreground. As Peterson

very justly says, if we are going to really cure the greatest possible number of our patients, such a frequent coincidence of what in many cases certainly amounts to a major pathologic condition must be met by a recognition of its importance, and a consciencious attempt to remove this pathology wherever it appears feasible. In somewhat less than half (57 out of 135) of the cases in which gall-stones are palpated in Peterson's series, were they actually removed, in the others the condition of the patient, or other conditions, rendering it apparently inadvisable to extend the original operation. Peterson has been able to trace a large proportion of cases of both classes, and has found that about 90 per cent. of those from whom stones were removed have remained since operation free from any symptoms referable to the gall-bladder, whereas only about 60 per cent. of the patients in whom stones were palpated, but not removed, have remained free of such symptoms. Peterson therefore concludes that if we do not consider the gall-bladder in our routine gynecologic operating, about 30 per cent. of our patients will be left with a symptom-producing residuum of pathology, from which in many cases they could have been relieved. Especially in this attention to the gall-bladder important, he has found, in women who have borne children, and who are of advancing years, both of which conditions are apparently important factors in the production of stones.

New Medium for Pyelography.—After citing a number of cases, reported in the literature, in which damage to the kidney tissue has followed the use of collargol or similar substances in order to obtain a Roentgen shadow of the renal pelvis, YOUNG (*Boston Méd. and Surg. Jour.*, 1915 clxxii, 537) says that all soluble preparations of silver are more or less irritating to mucous surfaces, and are therefore bound to cause a certain amount of irritation when applied to them in any degree of concentration. In the attempt to find a perfectly harmless, non-irritating substance for use in pyelography, he therefore turned his attention at once to the insoluble silver salts. Kelly and Lewis suggested silver iodide some time ago, but various attempts with it proved unsatisfactory, because of the difficulty of getting a medium which will hold the salt well in suspension, and at the same time be sufficiently fluid to be easily introduced into the kidney pelvis and drained out again. In conjunction with the pharmacist to the Massachusetts General Hospital, Young says that he has succeeded in evolving a menstrum which satisfactorily fulfils these requirements. It consists primarily of a thin quince-seed mucilage, with which is incorporated a definite amount of "argentide," an easily obtainable commercial product, consisting merely of a saturated solution of silver iodide of constant composition. (The details of the formation of the emulsion are given in the original article.) The resulting emulsion is a thin, clear fluid, which flows readily through a ureteral catheter, and which remains good for use for several weeks after manufacture. Young says that this substance has now been in use in the Massachusetts General Hospital for about three months, and has given entire satisfaction. No untoward after-effects have been encountered, and in a few cases in which nephrectomy has been performed subsequent to the pyelography no trace of the material could be found in the substance

of the kidney, and mere traces adhering to the pelvic wall. In no case was an injection of more than 3 c.c. necessary to produce a good shadow, although in some instances the capacity of the renal pelvis was 20 c.c. or more, so that the silver emulsion must have been greatly diluted. The author employs the barrel of a 10 c.c. syringe as a container, from which the solution is allowed to flow by gravity through the catheter. After the picture has been taken, the piston of the syringe is inserted, and as much as possible of the solution sucked out of the kidney pelvis, the larger part being thus recovered in most instances. The pelvis is then washed out once or twice with boric acid or salt solution.

Results with the Percy Treatment for Uterine Cancer.—For the past few years, Percy has been advocating a modified form of treatment of inoperable uterine cancer by heat, employing what he terms the "cold cautery," *i. e.*, an iron heated to a point not sufficient actually to char tissue, but only to disseminate through it an amount of heat which will kill cancer cells without affecting those of normal tissue. Percy claims that malignant cells can be destroyed by a temperature of 50° to 55° C., whereas normal cells require from 55° to 60° for their destruction. His endeavor, therefore, is to maintain the temperature of the cautery at about the lower of these figures, and to keep it in place for fifteen minutes to half an hour, in order that the heat may be thoroughly disseminated throughout the entire mass of malignant tissue, the vaginal walls being protected by a water-cooled speculum. In a recent paper, CLARK, of New Orleans (*Surg., Gynec. and Obst.*, 1915, xx, 558), reports some excellent results from this procedure, and especially emphasizes its usefulness as a preliminary to radical operation. He reports two cases which when first seen were considered entirely inoperable, but after a series of heat applications they were transformed to such a degree that radical operation was possible. Examination of the removed uteri, even by repeated serial sections, failed to reveal any cancer cells in either specimen. He says that he has two other cases in his hospital service which, after five and three treatments respectively, show such marked improvement, both constitutionally and locally, that it is believed a radical operation may be done. "In the border-line operative cases," continues the author, "the application of this extensive heat has a most gratifying result, making many operable that otherwise would have been declined. Whenever there is a definite ulceration with bleeding, having as a rule an associated local infection with slight infiltration, the Percy cautery should be employed as a preliminary measure, since it not only acts in destroying the infection, but stops bleeding and toxemia, and the case will in three weeks be a far better surgical risk than when first seen." Clark does not advocate the use of the cautery and the performance of a radical operation at one sitting, but thinks it is better to divide the procedure. He firmly believes, however, that a judicious combination of these two methods of attack will yield a higher percentage of permanent cures than either alone. In very early cases, where the patient is a good risk, he sometimes applies the cautery for about twenty minutes immediately before proceeding to a radical extirpation, with the idea of killing off the cancer cells, at least those near the uterus and within the vault of the vagina, thus avoiding the danger of grafting cancer cells when the abdomen is

opened. Clark emphasizes that this paper is merely in the nature of a preliminary report, since his experience with the method is barely two years old, but his results with it so far have been so encouraging that he wants to get others interested in it. With regard to technique, Clark follows that described by Percy himself, with a few minor modifications. He has had two cases of severe hemorrhage following the treatment, one of these ending fatally, and now ties the internal iliacs in order to avoid the possibility of this.

Artificial Impregnation.—Prochownik (*Zentralbl. f. Gynäk.*, 1915, xxxix, 145) says that in the course of a practice covering several decades he has made upon 13 individuals 21 attempts at artificial fertilization, with 3 successes. He emphasizes strongly the necessity for a thorough examination of both husband and wife, not only from the point of view of their general physical and sexual development, but also entering somewhat into the psychic field. Having determined the presence of apparently living spermatozoa in the seminal fluid of the husband, and the absence of mechanical obstructions to conception in the wife, Prochownik says that he now always demands permission for at least two attempts before undertaking artificial fertilization. The best time for this he considers between the fifteenth and twenty-second day after the beginning of the preceding menstrual period. He lays great stress on the importance of carrying out all procedures quickly, deftly, and without undue fuss and elaboration. He uses the ordinary Braun intra-uterine syringe, which should be warm and dry. Coitus is permitted with a condom; immediately following this, the semial fluid is drawn into the syringe from the condom, and not more than 0.5 c.c. injected into the *uterine cavity* (not merely into the cervix), the remainder being placed upon a sterile tampon against the external os. The woman is kept in bed for about an hour and a half, after which the tampon is removed, and she is allowed to resume her normal activities. Prochownik thinks that the mental attitude of the patient is of equal or greater importance than refinements of technique, hence the importance of a second trial if the first does not succeed, since the patient is apt to be much less nervous and frightened than at the first attempt.

Dysmenorrhea Associated with Ovarian Hemorrhage.—Whitehouse (*Jour. Obst. and Gynec. Brit. Emp.*, 1914, xxvi, 152) reports a rather interesting case of dysmenorrhea, in which the only demonstrable lesion was in the ovaries. The patient was forty years of age, unmarried, and had suffered throughout her entire mentrual life with severe pain at each period. This pain always began a few days before the onset of the flow, first over the sacrum, gradually extending to the flanks and hypogastrium. A dilatation of the cervix and curettement had been performed nine years previously, without relief. Physical examination was negative, but all medical measures failing to give relief, it eventually became necessary to remove the uterus, tubes, and ovaries. No inflammatory or other lesions were found, but on section both ovaries, which were about normal in size, appeared dark red in color, and studded with minute punctiform hemorrhages. The blood was entirely in the stroma tissue, none being found in the Graafian follicles or corpora

lutea. The hemorrhages did not appear to be all of the same age, the blood cells in some of the apparently older collections not staining well, and being partly absorbed. The operation was done in the premenstrual period. The author suggests for the condition the term "ovarian purpura;" as no inflammatory reaction was present, such a term as "hemorrhagic oöphoritis" would be inapplicable. The clinical association of the condition with acute menstrual pain is, he thinks, clear. He suggests that perhaps the cause of the hemorrhage may lie in a local developmental defect in the capillaries of the cortex, by which they are unable to resist the congestion taking place at each menstrual period, and says he is quite convinced that whereas in cases of severe dysmenorrhea, attention is generally directed to the uterus rather than the ovaries, the latter are frequently the seat of menstrual pain. He considers, therefore, that when drugs and other measures applied to the uterus fail to relieve, exploration of the ovaries appears to be justifiable and indicated.

OTOLOGY

UNDER THE CHARGE OF

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Treatment of Chronic Suppurative Disease of the Middle Ear by Means of Lactic Acid.—EITELBERG (*Wien. med. Wchnschr.*, 1914, 22) recommends the lactic acid treatment in cases of a moderate degree of engorgement of the tympanic mucosa with the presence of small polypi which either speedily shrink or come away as necrotic masses in the subsequent syringing of the ear. The result of the treatment is speedily apparent in the more favorable cases and the resultant pain from the application is usually slight, of short duration, and unaccompanied by prejudicial results. The application of the lactic acid is made, after thorough syringing and drying of the middle ear by means of a cotton tipped probe, dipped in a warm solution of equal parts of lactic acid and allowed to remain in contact with the affected parts, the head of the patient being so inclined as to bring the ear under treatment uppermost for a period of three minutes, after which the ear is dried by means of absorbent cotton and boric acid powder insufflated. This application may be repeated on alternate days and, as the suppuration decreases, the preliminary syringing may be dispensed with.

Treatment Consecutive to the Mastoid Operation.—In cases of uncomplicated acute mastoiditis DELSAUX (*Presse. Méd.*, 1914, xiii, 2) regards the primary stitch closure of the postaural wound as allowable only when there is a large perforation of the drumhead with ample assurance of drainage through the external canal and when, moreover, the post-operative treatment can be properly supervised, otherwise the post-operative treatment by packing is to be preferred. In chronic uncomplicated mastoiditis, after thorough

evacuation and removal of diseased tissues and completion of the plastic portion of the operation in the external auditory canal, the postaural wound is to be primarily closed and a light sterile gauze wick inserted into the external canal for the purpose of keeping the canal flap in place, this dressing being renewed every second day, or at longer intervals, until it is possible to dispense with it altogether and substitute insufflation of boric acid, or of lactol in powder form, or the insertion of a light gauze wick soaked in neutral vaseline or in albolene. In event of caries of the ossicles these should be removed as a precedent to the radical operation and, even in cases of cholesteatoma the author deviates but little from the postoperative procedure outlined for the cases of uncomplicated mastoid disease except that the, surgically provided, lumen of the external auditory canal should be made larger and that, as a provision against relapses, no islands of epidermis should be allowed to remain within the operation cavity. A persistent and, especially, a firm packing is prejudicial; in its place there should be the boric acid insufflation, but always carefully supervised, the accumulated powder being removed from time to time by means of syringing and the surface, which it has covered, minutely inspected, the tympanic end of the tympanopharyngeal tube carefully cleansed, granulomata cauterized, and all epidermal accumulations removed. Under these conditions the author has been able to discharge his cholesteatomatous patients to the out-patient department in from eight to ten days with resultant complete healing in from twenty to fifty days, an average period of after-treatment much shorter than that under the formerly customary firm packing.

Otitis Circumscripta Externa Simulating Mastoiditis.—Botella (*Archiv. Internat'l*, xxxvii, 3) makes distinction first between the circumscribed inflammation of the external canal and the more defined furunculosis, which is limited to the inflammation of a hair follicle and its immediate environment, and then draws attention to the superficial simulation of a mastoiditis due to extension of the dermatitis of the canal to the postaural space, originating in an infection in the canal, from a scratch wound for example, and implicating the subcutaneous connective tissue which constitutes the medium of communication from the external canal to the skin of the mastoid region with resultant edema, tenderness and localized abscess formation with fluctuation, suggestive of an inflammatory and suppurative process of deeper origin. As differential evidences the author draws attention to the fact that in the circumscribed inflammation of the canal the pain is severe but more superficial and increased by movement of the auricle, while pressure upon the mastoid surface, without touching the auricle, is unproductive of pain, that there is distinct evidence of swelling, redness and tension in the external canal confined to its cartilaginous portion and only secondarily implicating the dermoid surface of the bony canal wall and that the drumhead is not a participant in the congestion and inflammation. In mastoiditis the pain is more constant and more deeply seated, pressure upon the mastoid surface evokes a sensation of internal, as well as of external, tenderness and the swelling of the canal is principally upon the posterior superior wall and is evidenced

particularly in the bony portion of the canal, while the drumhead gives evidence of the implication of the middle ear. In the matter of treatment of the circumscribed inflammation of the canal the author recommends early and free incision and dressing with plain sterile gauze in perference to iodoform gauze because of the effect of the latter upon the usually accompanying eczema.

PATHOLOGY AND BACTERIOLOGY

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Leukocytic Bacteriolysins and Their Relation to the Alexin.—LEVADITI (*Bull. de l'Institut Pasteur*, 1914, xii, p. 481) has given a very comprehensive review of the work upon this subject. For many years active discussion has surrounded the problem of the origin of the bacteriolytic substances of the serum. Buchner contended that the leukocytes liberate them by active secretion, while Metchnikoff believed that the active substances were only liberated on the death of the leukocytes. Each of these views has had its followers. The problem has not alone an academic interest but, because of the newer suggestions for the therapeutic application of some of the principles involved a definite knowledge of the nature of the leukocytic enzymes is desirable. Levaditi has discussed the subject from various view-points. He compares the experimental results upon the bactericidal action of leukocytes *in vitro* and *in vivo*. Baumgarten claimed that the phagocytosis in the absence of a specific serum was an incomplete process in that the bacteria were not actually destroyed within the leukocytes. On the other hand, the majority of authors agree with Hektoen that the *in vitro* experiments upon phagocytosis demonstrate a definite destructive activity and that the experiments closely simulate the reactions of the body. Some *in vivo* experiments also establish a destructive process by the leukocytes of many forms of bacteria. Moreover, a definite relation has been established between the protective power of an individual and the height of a leukocytosis. From these observations the Metchnikoff school wish to contend that our immunity in general has a direct bearing to the leukocytic response. Many studies have been undertaken to determine the anti-microbic substances in leukocytes. For the most part, the substance is of a common kind, acting against a variety of bacteria. It has some simularities with alexin, but is more heat resisting than that body. The active substance of leukocytes is not of a lipoid nature, but is soluble

in water and has the character of a ferment. It appears from a number of experiments that the active substance can be preserved for considerable periods of time when kept in the dry state. Ordinary fresh leukocytes rapidly dried show bactericidal powers for several weeks. An interesting observation is recorded that the leukocytes of immunized animals are consideraby more active against the specific bacteria than normal leukocytes. The work is very suggestive and stimulates interest to follow the therapeutic application of leukocytic extracts as was suggested in Opie's work.

The Cellular Reactions Induced by Local Deposits of Cholesterin.—Recently much interest has been displayed in the significance of cholesterin in health and disease. It is a not uncommon finding during the routine examination of human tissues under pathological conditions to observe some form of cholesterin. STEWART (*Jour. Path. and Bact.*, 1915, xix, 305) has noted that cholesterin may appear in different physical forms, as well as give rise to different reactions in human tissues. Thus, both under normal and pathological conditions, cholesterin often appears in a peculiar type of cell, the foam cell, which deals with the cholesterin in combination with lipoids. True crystals of cholesterin are not to be observed unless the fatty compounds have been disturbed by the preservative. On the other hand, cholesterin also appears in tissues in the pure state as rhomboid crystals, bunches of fine needles or prisms. Such free cholesterin is not readily handled either by the cells or the tissue fluids. The crystals stimulate the production of foreign body cells and their presence in sections is distinguished by the clefts seen in the tissues. Frequently large cells surround these crystals and render them physically inert. At other times the cholesterin forms a rosette-like deposit. Many spicules radiate from a center producing curious masses. Here again giant cells commonly surround the deposit. Such deposits are found in the breast.

Symmetrical Cortical Necrosis of the Kidney in Pregnancy.—Since the first report of Rose Bradford and Lawrence 1898 of symmetrical cortical necrosis of the kidney, eleven more cases have been reported by the English and American authors. The condition is such a serious one that each new case assists in bringing to light new facts concerning the disease. GLYNN and BRIGGS (*Jour. Path. and Bact.*, 1915, xix, p. 321) record another in a primipara of 29 years. In the eighth month of pregnancy she aborted. There was almost complete suppression of urine for the next week and she died in coma. There were, however, no convulsions. At autopsy the kidneys were found to have the characteristic appearance described in this disease. The outer portion of the cortex was found to be of a lemon yellow color while the medulla was somewhat congested and a hemorrhagic zone demarcated the necrotic layer from the underlying tissues. The main vessels of the kidney were uninvolved but in the zone of demarcation a widespread thrombosis of blood plates was observed. The nature of this thrombosis has been the point mainly in question by the various authors. Some have described them as of fibrin, others of red blood cells, others of debris, while now a new suggestion of

platelets is offered. They believe that the condition may begin with injury to the vascular endothelium followed by thrombosis of the interlobular arterioles. It is not clear why this particular group of vessels should be picked out.

Teratoma of Anterior Mediastinum. — The unusual finding of a mediastinal teratoma is reported by PRYM (*Frank. Zeit. f. Path.*, 1914, xv, 181). The tumor mass, the size of a flattened orange, was removed at operation from the anterior mediastinum of a girl of eleven years. The mass was attached by a pedicle to the inner wall of a cyst which was clothed by epithelium. Incomplete removal of the cyst wall led to a recurrence of the cyst. The tumor mass was amorphous, covered by epithelium and long hair, and having several teeth on one surface. Bony structures were contained within it. There are seven other reported mediastinal teratomata in which teeth were found, while in only two did the bony structures resemble the mandible. On account of the similarity between the mediastinal tumors and those of the ovary the author believes that the blastomere theory of Marchand is best adapted. By this it is suggested that in the early history of the embryo polypotential blastomeres become misplaced.

Myocotic Aneurysms of the Aorta with Perforation into the Œsophagus.—New cases are constantly being added to the relatively long list of mycotic aneurysms and with the new reports attempts are being made to classify the nature of the process and the manner in which the serious outcome is brought about. There have been at least five suggestions as to the mode of localization of the infection upon the aortic wall: (1) extension of an inflammatory process from an external neighboring infectious process; (2) a metastatic deposition upon the aortic intima from valvular endocarditis; (3) a lymphatic distribution into the wall of the aorta; (4) infection of the media by an invasion through the vasa vasorum; (5) infection of the surface of the intima from a distant focus. EDENHUZIEN (*Frank. Zeit. fur Path.* 1914, vol. 16, H. 1) reported two new cases of this disease, in the first of which he suggests another mode of infection. The case was one of an acute septic process in diabetes which led to the localization of the infection in the arteriosclerotic plaques of the aorta. It is suggested that the invasion took place upon the intimal surface and then progressed deeply into the wall of the aorta. Perforation without the development of a sacular aneurysm took place into the œsophagus. In the second case a tuberculous process extended from the outer portion of the aorta until the weakened wall ruptured into an erosion of the œsophagus. The tuberculous process progressed relatively rapidly in its destructive lesion of the aorta and the neighboring tissues.

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